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Linking Competition to the Economic Incentives for Firms to Innovate

In the Context of the U.S. Pharmaceutical Industry

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Abstract

The main purpose of this research was to investigate the economic incentives for firms to innovate and to show how competitive forces might influence these incentives. It was predicted that the correlation followed an inverted U-shaped relationship.

To do so it was necessary to take some initial steps before it was possible to investigate this correlation. First and foremost the objective was to raise the product evaluation of an innovation to higher level than on the product itself. Hence, the study sought to show if new product innovation influenced the firm as a whole – i.e. the overall expected firm performance. To do so it was vital to bridge economic innovation with the ideas of financial markets. By accepting the Efficient Market Hypothesis (EMH) in its semi-strong form and by relying on the Principle of the Conservation of Values, new information regarding product innovation *must* be reflected efficiently in a firm's security prices as soon as this information becomes publicly available. If the connection is successful and efficient the expected firm performance in relation to new product innovation serves as valid approximation to the economic incentives for firms to innovate. The connection can be established via the event study methodology.

Using the pharmaceutical industry as this study research context, the study successfully connected economic innovation with financial economics via an event study. The pharmaceutical industry was chosen because it possesses the necessary conditions to conduct an event study, and because the industry itself has gone through some interesting changes in relation to competitive implications. The event study showed that the expected firm performances (abnormal returns) from new innovations (drug approvals) were reflected *somewhat* efficiently in the firms' security prices. The expected firm performance related to these product approvals consequently serves as a valid approximation to the economic incentives for firm to innovate.

With a valid approximation, this study showed that increased competition, at least in more recent time periods, has a positive impact on the firms' economic incentives to innovate, however, only up to a certain point. The study showed that excessive competition has an economic disincentive for firms to innovate once a certain threshold was met. In conclusion, the study showed that the economic incentives for firms to innovate and competition follow an inverted U-shaped relationship as predicted. These findings might prove to have practical implications from a shareholder perspective as well as to have implications to effective policy reforms.

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1. Introduction

Does innovation pay off? For many years this question has been studied in a vast variety of theories and approaches. Is innovation just a constant flow of product introductions to catch up to or to leave the way for new ideas or processes, or is innovation derived from a more fundamental difference between firms (and people)? Is innovation embedded in some firms' internal capabilities rather than others? Sometimes innovation is linked to entry-deterring behavior or simply a reaction to competitive pressure to sustain a competing edge. These are just a fraction of research angles to the current literature regarding economic innovation.

1.1. Background

The motivation for an innovator to engage in the unknown; to disrupt stability in equilibrium might not "only" be a tempting promise of earning an above average return. According to the founding father of economic innovation, Schumpeter (1912), the innovator is no ordinary businessman; rather he is a businessman with the ability to initiate and to dare to overcome all obstacles to innovate in steady equilibrium – or as he labelled the "circular flow". The circular flow is characterized by allocating resources efficiently. This ought to create uncertainty for the entrepreneur's possibility to earn a significant return on his innovation, even more so when it comes to how his new innovation might influence the performance of his new firm as a whole.

Ex-ante uncertainty, however, is what creates value for a new "discovery" or a new "invention" (Rumelt, 2005). Hence, profit relates to risk and uncertainty, as "the presence of true profit depends on an absolute uncertainty in the estimation of the value of judgement" (Knight, 1964, p. 285). Risk can be accounted for but, without uncertainty, rivals can expect the entrepreneurial investment to reflect its true value and no obstacles for imitation will be present.

The idea of the "perennial gale of create destruction" whereby new innovation replace older ones indeed creates a luxurious condition for the entrepreneur, at least for a period of time (Schumpeter, 1942). With a successful novel product introduction, the entrepreneur enjoys a period of abnormal profits as consequence of limited competitive pressure.

Innovation however, tends to come in clusters, because of herd-like actions from followers in the wake of successful product introductions. Hence, innovations come in "wave-like movements" as a swarm of imitators follow the success of one innovation in the hunt for exploitation of any "entrepreneurial rent" created by the initial innovation (A. H. Hansen, 1951). The host of followers absorbs any abnormal return created by the initial innovation, and competitive forces eventually

drag the "economic development" of innovation back to a steady equilibrium – the circular flow until the next wave of innovation shocks the market. Recent empirical findings support this constant wave-like movement of economic life arose by the appearance of an innovation which subsequently ignite the herd-like actions from imitators moving the economy from one equilibrium to a new one (e.g. (Geroski, Machin, & Reenen, 1993; Roberts, 1999)). Hence, economic abnormal profitability created by innovations is only transitory, as competitive forces eventually pull the economy back toward equilibrium.

If competition then ensures no abnormal return for innovative behavior in the long run, is competition only a barrier for innovative activities to thrive? Schumpeterian supporters and theories claim that more competition everything being equal harms the incentives to innovate as the post-innovation rent decreases with higher levels of competition (Dixit & Stiglitz, 1977; Romer, 1990).

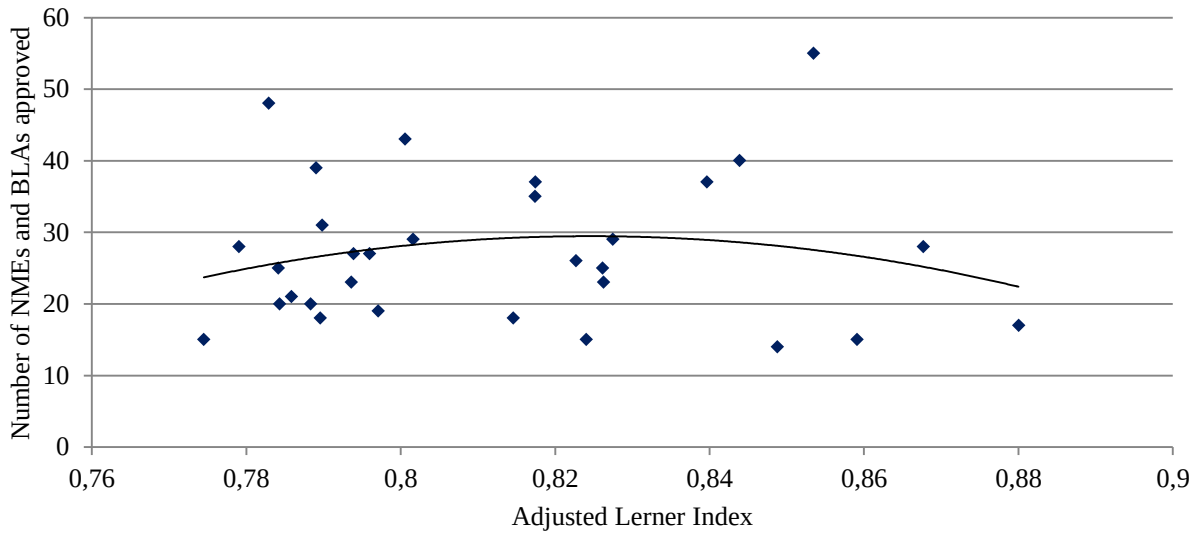
Empirical evidence however points in an opposite direction, where competitive forces are the main driver for innovation either as an anti-competitive behavior (Gilbert & Newbery, 1982) or to keep an competitive edge – to "stay in the game" (Arrow, 1962).

Some scholars even displayed an inverted U-shaped relationship between competition and innovation (Aghion, Bloom, Blundell, Griffith, & Howitt, 2005). By allowing for pre-innovation rent in models[1], incumbent firms are now stimulated to innovate as competition increases. A behavior labelled as "escaping competition", which thrives particularly in industries with low initial level of competition and competing products approaching the technology frontier. In industries characterized by higher competition, adding even more competition will have a less positive effect on innovation or even have a negative impact once a certain competition threshold is met – i.e. the "Schumpeterian effect" is dominating.

The latter theory connecting competition and innovation seems rather compelling. In fact when plotting the number of innovations, here as measured in the amount of new drug approvals in the United States, against some measure of competition, it seems evident that there appear to be an inverted U-shaped relationship between innovation and competition. Figure 1 shows that the number of new innovation approvals is an increasing function of competition, at least until a certain threshold is met.

[1] Most Schumpeterian models do not account for pre-innovation rents from the incumbent firms. In these models only post-innovation rents are presents, where entrants are drawn to the attractiveness or size of the post-innovation rents.

Figure 1: Scatter Plot of Number of Approved Drugs on Competition



Note: The competition measure in Figure 1 is the adjusted Lerner index – a profitability measure. A value equals 1 indicates full competition. A value below 1 indicates some level of monopoly. The number of approved drugs was recorded from 1985 to 2015.

Despite an already well-established literature connecting competitive implications on innovation, yet empirical evidence linking the value of new innovations on the overall firm performance, and in particular show how competition might affect these performances is rather limited. Prior research to a large extent investigated under what market conditions innovation thrives in terms of R&D output as measured in the number of patents (Blundell, Griffith, & Van Reenen, 1999) or on the overall productivity growth for firms (Nickell, 1996).

Other studies assessing innovation performances fail to lift the evaluation higher than on the product itself. For instance, Cooper & Kleinsmidt (1987) investigated factors that separated product "winners" from "losers". However, all factors to success determinants were based on the individual performance of the product, including product advantage, market potential or marketing synergies. Zirger & Maidique (1990) investigated what factors differentiated successful product development efforts from unsuccessful counterparts in the electronics industry. Again, factor determinants to product success, like the technical performance of the product, the product's value to the customer and product synergies, where all evaluated on the product itself.

As pointed out by Sharma & Lacey (2004) the majority of existing literature assesses performances of a new innovation on a product level only, omitting the possibility that new innovation may not influence the performance of the firm as whole. After all, if firms' investment

activities fail to materialize into shareholder wealth gain, what is point – at least for publicly traded companies?

When studies occasionally investigated the correlation between new product innovations and overall firm performances (e.g. (Bosch & Lee, 1994; Sarkar & de Jong, 2006), they fail to explain any reasonable implication to why expected firm performances might increase to new product innovation – including to what extent competitive forces might influence these expected firm performances. From a practical point of view, how should shareholders react to increased competition – should they buy more shares or should they sell?

The main motivation behind this paper is to investigate the "missing" link between the effects of new innovation on the expected performance of the firm as a whole, and how competitive developments might affect these performances. Hence, the motivation is to show how competition might affect the "economic incentives for the firm to innovate". The economic incentives are however two folded and require some explanations. The expected firm performance in relation to new innovation is implicit a measure of the market's perception of how a specific innovation will affect the expected performance of the firm in the future. If a new innovation increases the fundamental values of a company, shareholders will reward a firm's innovation efforts by increasing its firm value – hence, it serves as an economic incentive for shareholders to inject new capital into the firm to receive a share of the economic gains brought by the new innovation. This assumption relies heavily on the Principle of the Conservation of Values – i.e. corporate activities that "does not increase cash flows does not create value" (Koller, Goedhart, & Wessels, 2010, p. 24). Hence, if new innovation increases firm values, this new innovation must create value for shareholders.

This in turn increases the economic incentives for the firm to innovative as it increases shareholder value – i.e. the main objective for a given firm. The incentives to innovate thus become a continuous and accelerating cyclical process at least as long as the incremental profit from innovating is positive – i.e. as long as innovation creates value.

This raises product innovation to become more than just to show a positive net present value, but rather to investigate if product innovation has financial implications beyond the product itself. In addition, this study attempts to investigate how innovation incentives might change with the levels of competition.

The theoretical arguments of this paper adopts the theory proposed by Aghion et al. (2005). They hypothesized and empirically proved an inverted U-shaped relationship between innovation output, measured in the number of patents, and competition. Translating their inverted U-shaped relationship to the economic incentives for firms to innovate, it is predicted that the economic innovation incentives follow an inverted U-shaped correlation with competition.

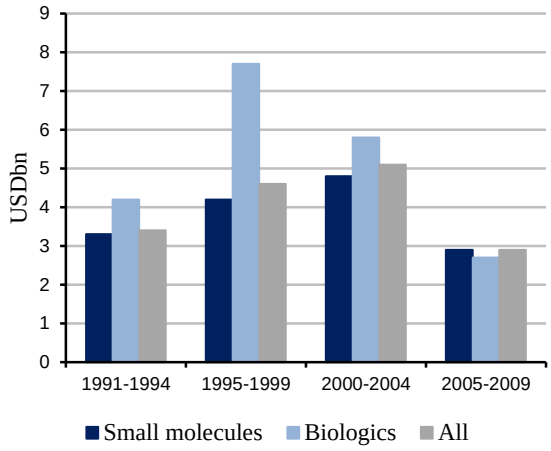
To investigate the competitive implications on the economic incentives for firms to innovate, it is essential to link the finance literature with economic innovation. This connection can be established via the event study methodology and the above investigation becomes a question under the umbrella of the Efficiency Market Hypothesis (EMH) – at least when it comes to bridging product innovation and the economic incentives for firms to engage in innovation. With the connection established it opens up for the possibility to assess the impact of competition on the expected firm performances.

When connecting economic innovation with the idea of financial economics, the study will consequently be constrained to event-study-available data. To overcome this issue the pharmaceutical industry was selected as this study's empirical context.

The pharmaceutical industry was chosen as this study's empirical context for two reasons. First and foremost, the pharmaceutical industry possesses the necessary conditions to carry out an event study. Product approvals in the United States are clearly marked events controlled by the Food and Drug Administration (FDA) that serves as a crucial gatekeeper for the North American market.

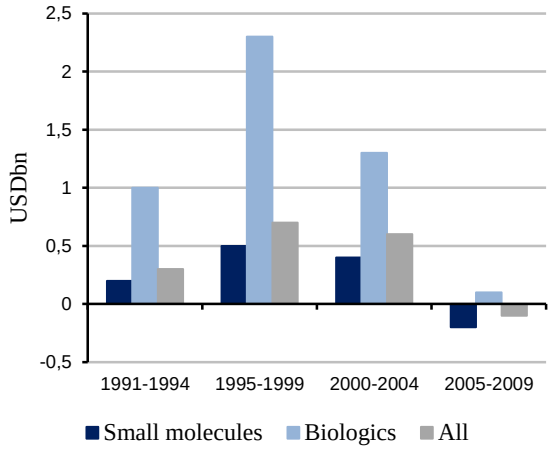
Second, the industry in the US itself has gone through some interesting changes for the past 30 years. The enactment of the Hatch-Waxman Act in 1984 allowed generic competition in to the market, which put a downward pressure on the incumbent pharmaceutical companies that has been enjoying a prolong era of economic growth. Figure 2 and Figure 3 sum up the development of the pharmaceutical industry broadly – at least from 1994 to 2009. Figure 2 displays the average present value of sales of branded drugs that up until the 2000-2004 cohort had experienced a growing trend. However, when looking at the overall net economic returns (Figure 3), branded drugs had shown a negative trend since the 1995-1999 cohort and even turned negative in 2005-2009 cohort. A great proportion of these changes can be attributed to increase generic competition.

Figure 2: Average Present Value of Lifetime Global Net Sales of Prescription Drugs



Source: (Berndt, Nass, Kleinrock, & Aitken, 2015)

Figure 3: Average Lifetime After-tax Net Economic Returns of Prescription Drugs



Source: (Berndt et al., 2015)

Hence, the pharmaceutical industry provides a suitable framework to investigate what implications increased competition might have on the expected firm performance in relation to new product innovations and hence, the economic incentives for firm to innovate.

1.2. Research Question

Inspired by the framework developed by Aghion et al. (2005) and with the pharmaceutical industry as this study's empirical context, the study is set up to answer the following research question:

How do competitive forces affect the economic incentives for firms to innovate?

1.3. Study Outline

The study begins with a literature review of existing theories and empirical studies in relation to innovation, and how competition influences the incentives for firms to innovate. A pharmaceutical industry analysis follows to give the reader a broad insight into the development within the pharmaceutical industry as well as to put some perspective to why this particular industry was chosen as this study's research context.

The theoretical arguments and the general expectations for the research question will be discussed in the Theoretical Framework section followed by the establishment of two vital

hypotheses that enables to current study to answer the overall research question. The Methodology section introduces the methods used to test the established hypotheses, which are followed by the main findings in the Event Study Analysis and the Regression Analysis sections. A conclusion and a discussion of the main the findings end this study.

2. Literature Review

In this section the literature of existing theories and studies within economic innovation is reviewed. First, the main motivation for innovation is discussed, followed by how competing theories predict the relationship between innovation incentives and competition.

2.1. The Incentives to Innovation and Abnormal Return

The founding father of economic innovation, Schumpeter (1912) argued with the introduction of an innovative product, limited direct competition ensure a relatively high or abnormal profit for the entrepreneur – a concept he later referred to as a process of creative destruction (Schumpeter, 1942), where new innovation replace older ones. However, corresponding abnormal profits as a reward for new innovation tends to fade away as imitation and competition are swarming the market space in the wake of the success of the initial innovation.

Studies have since investigated the correlation between innovation and firm profitability. Geroski et al. (1993) measured how production of major innovations affect the profitability of innovation-producing firms, more specifically whether the correlation between innovative output and profitability reflect transitory or permanent performance differences between innovating and non-innovating firms. An interesting proposition is attached to this question, as it corresponds to two different views on why innovation can generate superior performance. One view is the *product of the innovative process*, where superior performance is created because new innovations affect a firm's market position in terms of a better competitive position than rivals. The second view is the *process of innovation*, which means that new innovations themselves transform a firm's internal capabilities in terms of building up or re-establishing core competencies. Geroski et al. (1993) were essentially looking at whether the production of innovations is transitory (the product view), as rivals eventually will successfully imitate innovator's innovations and erase abnormal profit until the launch of the next innovation cycle, or whether innovations are permanent and associated with generic differences between innovators and non-innovators (the process view). With a sample of

721 large UK firms, they showed that the number of innovations produced by a firm had a direct positive effect on its profitability as measured by higher profit margins, which supported the view of the product of the innovative process. More interestingly they showed that there existed a weak permanent profitability difference between innovating and non-innovating companies, and they concluded that this, perhaps more as a possibility rather than exclusively, reflected a more generic difference in the competitive ability between the two types of companies.

In a similar vein, Roberts (1999) developed and tested a framework for firm-level profit persistence with focus on product innovation, product-market competition and particularly the prospect that numerous product innovations can be embodied within a single firm. Roberts (1999) looked at how some firms can sustain high profitability over time with two competing explanations: an innovative explanation and an anti-competition explanation. Superior profitability in the former explanation can even occur in industries with relatively intense competition. Abnormal returns here are only transitory but with firms successfully introducing multiple innovations over time, they are able to sustain superior performance. The latter explanation relates to product introductions that in various ways fend off competition that would otherwise erode abnormal profits (e.g. entry-deterring behavior etc.). This explanation is consistent with the mind-set of that of the industrial organization economists. Based on the two explanations above, Roberts (1999) then hypothesized that persistent high profitability is positively correlated with a firm's ability or propensity to innovate (the innovative explanation). He further hypothesized that everything else being equaled more intense competition faced by innovative products over time should lead to less profit persistence and lower long-run profit levels (the anti-competitive explanation). In conclusion Roberts (1999) found a significant link between the level of innovative propensity and persistent abnormal returns over time; however his analysis provided weak empirical support for the theoretical framework behind the anti-competition explanation.

The studies above showed that innovation indeed lead to abnormal profit, but the studies made an implicit assumption: superior profitability generated by innovations, are only temporary, with no or little support that superior profitability is somewhat embedded in a firm's internal capabilities. Over time profits driven by innovations will be squeezed out by competition and imitators, and only companies that are able to generate a serious of innovative products resulting in a series of mini-monopolies at a product level win the battle of persistent innovation (Geroski et al., 1993).

The interesting question related to this issue: how does competition impact innovation incentives and its ability to create abnormal returns?

2.2. Competition, Innovation and Abnormal Profit

In this section three competing theories link innovation incentives to competition: Schumpeterian theories, the theory opposing Schumpeter, and a theory somewhat combining the two. Despite opposing each other in many ways, these theories have one thing common – their dissension to the neoclassical theory of the firm. The theory review briefly describes the neoclassical approach. Furthermore, the managerial implications to competition is supplemental to at least two of the main theories, however a whole section has been devoted to these implications as they represent an important factor when deriving the main hypotheses.

2.2.1. Neoclassical Approach

Incorporating competition into the equation of innovation, many competing theories about this correlation and its impact on a firm's profitability have been discussed thoroughly. They are often distinguished between whether competition is "static" or "dynamic". Competition in the neoclassical theory of the firm, often recognized with the state of perfect competition, is static. Based on the static approach to perfect competition, characterized by perfect and costless information, profit and utility maximization and people behaving rationally, all models draw attention to the same focus on the long-run equilibrium. Once all firms eventually arrive at this point the economy is in a so-called steady-state equilibrium (Lipczynski, Wilson, & Goddard, 2013). Hence, competition here is defined by each firm in the short run to adjust its output in reaction to changes in market prices and costs of its resources and in the long run adjust the scale of its plant, so that in the long run each firm produces the quantity at which the market price equals long-run marginal costs (Hunt & Morgan, 1995). In this state there are no abnormal profits earned. Little room is made for innovation as the environment or the structure of the industry deteremines the conduct and performance of a firm. Hence, innovations (or organizational changes in firms) only occur as a respond to competitive pressure. In many cases innovation is not even accounted for in most models taking the static approach to competition.

The theorical framework of this study in general distance itself from the static view of competition. How can innovators have any incentives to innovate when the expected return is zero profits (Rumelt, 2005)?

Discontented with the static view of competition, some researchers rejected the neoclassical theory, and developed a more dynamic approach with innovation as a key driver for the dynamic movements of competition. Intresting discussion in this context is the relationship between competition and innovation and whether innovation is fostered by pre-innovation or post-innovation rents (or both).

2.2.2. Schumpeterian Theories

First inspired by Schumpeter (1912); he introduced a new way at looking at the economic process that strives for new equilibrium after an economy has been disrupted. He divided these processes into a static and a dynamic approach. He labelled the static process as the "circular flow" that constantly seeks an equilibrium state categorized by optimal allocation of resources. Once at this state, the nature of the circular flow prevents the equilibrium from changing. The dynamic process, which he labelled as the "economic development", occurs more naturally, derived from the economy itself with the entrepreneur as the disruptive element to the current stable equilibrium.

To disrupt the current state, banks play a significant role in the dynamic process. Giving credits to entrepreneurs allow them to create new businesses with newly employed production factors that in a stable equilibrium[2] have to be appropriated from old businesses. Hence, by allowing banks to provide credit on demand to innovators, the economy becomes dynamic as new businesses and products replace older ones.

It is important to note that Schumpeter's interpretation of dynamic changes stems from the innovations introduced by new firms rather than incumbent firms in the circular flow. Furthermore, through his concept of "creative destruction", new product innovations replace older ones. However, new innovations come in wave-like movements as imitators swiftly follow the success of one innovation (Schumpeter, 1942). The promise of high profits tends to attract imitative behavior in the wake of the success of the initial innovation, and over time competitive forces absorb all available abnormal return.

Based on his ideas of an economic development condition, Schumpeter estimated a negative linear relationship between competition and innovation. In his early arguments about competition, he referred to competition in the post innovation market, where all innovations stem from new firms (Schumpeter, 1912). Everything else being equal, lower levels of competition leads to higher levels

[2] Under the assumption of full factor employment

of post-economic rents, implying greater incentives for outsiders to enter the market through innovations.

Subsequent industrial organization theories and models accepted the Schumpeterian view of competition and innovation in various ways. In their model, Dixit & Stiglitz (1977) argued that higher product market competition reduces the post-innovation rents that consequently squeeze out the incentives for outsiders to innovate. Economists developing the new generation of endogenous growth models share the same view. An essential part of Romer's (1990) growth model assumes that increasing competition has a negative effect on productivity growth that in turn reduces monopoly rents. In this sense monopoly rents are the reward for innovators to innovate.

Variations to the Schumpeterian interpretation have also been carried out by scholars and argued by Schumpeter himself (Schumpeter, 1942). In his later work, Schumpeter argued that incumbent monopolists were the main drivers of innovation, as they possess the necessary internal capabilities to innovate – a concept he labeled as "routinized" entrepreneurship. Furthermore, firms in monopoly markets face fewer market uncertainties and possess a more stable cash flow to fund innovation (Du & Chen, 2010). Although, Schumpeter changed the agents of innovation from new entrants to incumbent monopolists, he still argued for a negative relationship between competition and innovation.

2.2.3. Opposing Schumpeter

Schumpeterian views, however, were often contradictory to empirical evidence. E.g. with 4,378 significant innovations introduced in the UK between 1945 and 1983, Geroski (1990) found no significant evidence that monopoly power stimulates the incentives to innovate, but rather reduce the rate of innovation. Another study by Blundell et al. (1999) revealed that industries with less competition, as measured by lower import penetration and higher concentration levels, had fewer aggregated innovations. Additionally, Nickell (1996), though not backed up by any theoretical framework but rather inspired by real life examples, found a positive relationship between increased competition and higher rates of total factor productivity growth, and hence innovation.

One of the first cited scholars to develop a model for this phenomenon was Arrow (1962) who modelled a linear positive relationship between competition and innovation. In his model the pre-invention, monopolistic power acts as a strong disincentive to further innovate, and the incentives to innovate under competitive circumstances always exceed the incentives for the monopolist. The

idea behind the proposition is that competitive forces are the main drivers of innovation for firms to keep a competitive edge – i.e. to defend or capture market share.

Empirically, Gilbert & Newbery (1982) showed that the R&D incumbent monopolists have a larger incentive to innovate. Introducing an efficiency effect in their auction model, they showed that innovations from incumbent monopolists worked as an anti-competitive mechanism to keep potential entrants from innovating. Incumbent monopolists are well aware of the destruction of abnormal profits or monopoly rents when more companies share the market.

An important difference between Schumpeterian supporters and Arrow (1962) is worth noting. While the former refers to competition in the post-innovation market the latter refers to competition in the pre-innovation market (Du & Chen, 2010). Both arguments may not conflict depending on what angle of interest is undertaken.

By looking at the organizational context of entrepreneurial activities, Rumelt (2005) argued that profitable incumbent monopolists have the least incentives to innovative due to the problem of cannibalism. The gains from innovating for incumbent are disrupted by the destruction of established rent payments from existing products. More importantly, the higher the entrepreneurial rent from older products, the lower the incentives for the incumbent to innovate. An important requirement for the cannibalism is the crucial asymmetries in customer responses. Many customers establish loyalty to a specific brand or company. Based on this argument of cannibalism, innovations are often introduced in direct response to an incumbent's unwillingness to innovate. Hence, innovation stems from potential entrants who then leapfrog passive incumbent firms.

In Rumelt's (2005) mindset, competition still plays a vital role as it reduces the isolation mechanism – a mechanism that protect innovation against imitative competition. Some sort of protection mechanism has to present before a risky venture can earn rents. Furthermore, he argued the competitive forces themselves are the innovative activities that together move industries or segments through the industry lifecycle.

2.2.4. Inverted U-Shaped Relationship

A third and more recent theory of the relationship between innovation and competition predicts the correlation between the two follows an inverted U-shape. It was first introduced by Scherer (1967) by allowing non-linearity (as opposed to Schumpeterian theories' and Arrow's (1962) linear

relationships). Based on the concept of a threshold effect once a certain level of concentration was reached in an industry, Scherer allowed the relationship to be non-linear. Built on the idea of non-linearity, Aghion et al. (2005) developed a rather compelling theory of the inverted U-shaped relationship between competition and innovation. In their theory both current technology leaders and their followers can innovate in a "step-by-step innovation model", where laggard firms have to catch up to with the market leaders in a given industry. Instead of isolating the incentives to innovate to only depend on the post-innovation rent, as opined by early Schumpeterian theorists, where all innovations are made by potential entrants, they model the incentives to innovate to depend on the difference between post-innovation and pre-innovation rents of incumbent firms (or as they labelled net-innovation rents). By focusing on the difference between the two sources of rents, competition might promote innovation and growth because it might reduce a firm's pre-innovation rents by more than it reduces its post-innovation rents. A situation they call "escaping competition", where "competition may increase the incremental profits from innovating, and thereby encourage R&D investments" (Aghion et al., 2005, p. 702), as opposed to the Schumpeterian effect that reduces only the post-innovation rents[3]. Hence, incumbent firms, in neck-and-neck[4] sectors, might be better off increasing R&D investments to escape competition from potential outsiders. They hypothesized that in industries with relatively low levels of competition the tendency of a neck-and-neck competing-situation between incumbents is often the case. In these situations the escaping competition effect is dominating, and consequently fosters innovation as increased competition lowers the incumbent pre-innovation rents more than it lowers the post-innovation rents. Hence, one can expect a positive relationship between competition and innovation. Contrary, in industries with intense competition, laggards firms with low initial profits tend to perform the majority of innovations, which in turn decreases only the post-innovation rents. In this situation the Schumpeterian effect is dominating, and hence one can expect a negative relationship between competition and innovation.

Aghion et al. (2005) confirmed the inverted U-shaped relationship between innovation and competition with empirical evidence comprising U.K. panel data using a flexible non-linear estimator. In addition they find a negative correlation between the degree of "neck-and-neckness" among firms and increased product market competition. Furthermore, they concluded that the

[3] In models where innovation is only introduced by laggard firms, pre-innovation rents are always equal to zero.

[4] Aghion et al. (2005) define neck-and-neck situation as incumbent firms competing with similar technological-based products. Hence, competing products approaches the technology frontier in these environments.

higher the degree of "neck-and-neckness"-type of situations in industries, the steeper the inverted-U shaped correlation between product market competition and innovation.

2.2.5. Managerial Implications on Competition

Hart (1983) proposed a different view between firm behavior and competition. He argued that increased competition is a source of discipline that reduces the amount of slack in the system that is not fully optimized, as individuals are not minimizing costs. Taking the analogy from microeconomics, where inefficiency occurs when marginal prices are larger than their marginal costs, the inefficiency in a managerial theory perspective takes the form of managerial slack. Given the separation between ownership and control in firms, managers have the opportunity to pursue what is in their own best interest including maximization of managerial incomes or effort minimization. This is in direct conflict with the profit or market value maximization - i.e. the primarily goal for the owners of the firm. This is also known as the principal-agent problem. Machlup (1967) claimed that managerial slack only exists if product markets are imperfectly competitive. Hence, in a market with increased competition, managers are forced to maximize profits (and hence minimize managerial slack) to survive. He further argued that greater competition not only reduces slack, but sometimes even eliminates it. In the model presented by Hart (1983) he concluded that in a competitive environment, when costs of one firm fall, then so do those of other firms. As costs fall, only profit-maximizing firms expand which in turn lowers the product prices and gives the managers in non-profit-maximizing firms less opportunity to pursue his or her own best interest. Hence, average managerial slack is lower in competitive environment than if there is only one non-profit-maximizing firm in a market.

Jacobsen (1988) agreed that competitive advantages as a result of innovation and the corresponding abnormal returns eventually dissipate over time. But instead of making an implicit assumption on the rate of convergence of profits once exposed to competition, as many researchers do, Jacobsen (1988) investigated the persistence of abnormal profits, and what strategic decisions innovating companies might undertake to sustain a comparative advantage. Remarkably, he found no correlation between market concentration and profitability, but instead found that managerial efforts, such as vertical integration, market share, and marketing expenditure intensity slow the convergence rate of abnormal profits. Hence, as argued by Hart (1983) and Machlup (1967), management reacts to competitive pressure, as they are well aware that their own best interest is

jeopardized if firm profits go below the acceptable rate of return. In that sense the managerial self-interest and the firm's profit maximization interests come to be the same once more competition is introduced.

Despite various efforts of management to implement strategic initiatives to sustain a persistent abnormal profit, Jacobsen (1988) concluded that eventually competitive forces dissipate these abnormal returns, and hence joins the thinking that the existence of abnormal returns exist with the proposition of a disequilibrium phenomenon.

2.3. Innovation in a Pharmaceutical Industry Context

As indicated in the Introduction, the pharmaceutical industry is selected for this study's research context. It is thus important to put the above incentives innovate in to context of the pharmaceutical industry in order to establish a meaningful theoretical framework for the current study.

Putting the incentives to innovate in to context of the pharmaceutical industry, patent exclusivity for a new drug makes it likely for the sponsoring firm to achieve a first-mover advantage. According to Rumelt (2005), a first mover advantage is an isolating mechanism of the innovation, which in turn is necessary for the companies' willingness to engage in entrepreneurial investments. Lieberman, Montgomery, & Wiley (1988) defined first-mover advantages "in terms of the ability of pioneering firms to earn positive economic profits" (Lieberman et al., 1988, p. 41). The presence of some initial asymmetry among competitors is critical. Without it, first-mover advantages cannot occur. In relation to the pharmaceutical industry, technology advantages are often defined as a function of R&D expenditure and once technology output is patented, pioneers can obtain a significant advantage.

In addition, winning the patent-race often allows pioneers to enjoy economic profits and breathing room from competition. The latter is significant in the pharmaceutical industry, where pioneers in other industries only obtain weak protection, as imitators can easily invent around patents. Gilbert & Newbery (1982) were the first to develop a model of pre-emptive patenting, where they proved that a firm with a significant head start in R&D expenditure is able to prevent rivals from joining the patent-race, and hence enjoy abnormal returns as a function of the lifetime of a given patent. However, to stay competitive, pioneers have to constantly improve products (Birnbaum-More, Weiss, & Wright, 1994), or continuously introduce a series of new innovations as

competition eventually absorbs all abnormal profits created by innovations (Geroski et al., 1993; Roberts, 1999).

Putting patents into the context economic innovation and competition, they serve as a protection factor of post-innovation monopoly rents (Aghion et al., 2005; Aghion, Howitt, & Prantl, 2012). As indicated above, in their step-by-step innovation-model, the incentives to innovate stem from the gap between pre-innovation and post-innovation rents. Thus, in situations with a neck-and-neck stage of competition (often present in less competitive environments), greater competition tends to lower the pre-innovation rents and in some cases also post-innovations, but the gap between the two sources of rent may increase even more so when patents protect the post-innovation rents. In these situations, patents increase the incentives to innovate as competition intensifies.

However, it is not a given that new drug approvals will be profitable for the sponsoring firm, in some cases far from it. To understand this implication it is important to understand the dynamics of the pharmaceutical industry.

2.4. Pharmaceutical Industry Analysis

The next section analyzes the pharmaceutical industry and its development over time. It gives the reader a broad understanding of the most important dynamics behind the industry as well as to give a logical explanation to why the industry is suitable as an empirical context to answer the abovementioned research question.

2.4.1. R&D Expenditure Growth and Declining Productivity

Most commonly, R&D productivity is defined as the ratio of input (R&D expenditures) versus its output (numbers of patents achieved or new product sales).

Looking at the overall cost structure in the pharmaceutical industry, then R&D expenditure is by far the biggest cost factor as seen in Table 1.

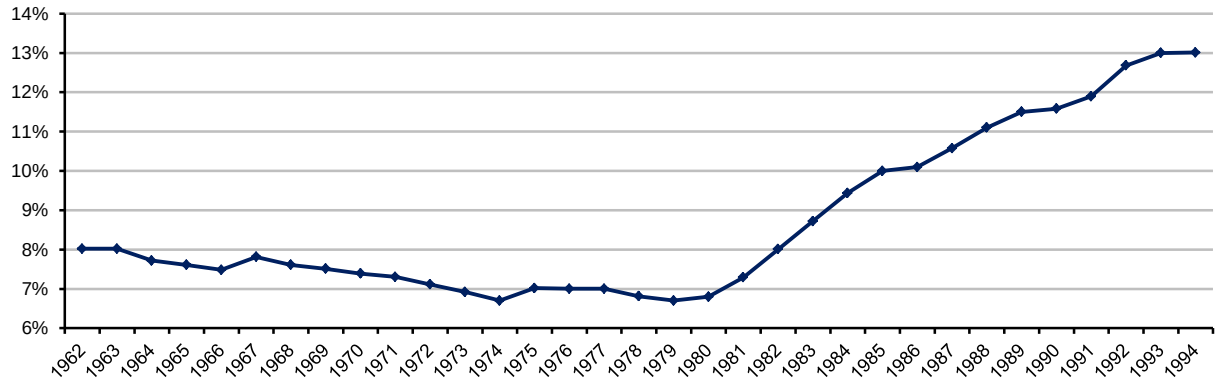
Table 1: Average Cost Structure of a Newly Developed Drug

Cost factors	Relative contribution
R&D, licenses	20–40%
Production	15–30%
Administration costs	5–15%
Marketing & distribution costs	20–30%
Margin	20–35%

Source: Gassmann et al. (2008)

Furthermore, these costs have been growing rapidly in recent decades from 8% of sales in 1970 to more than 13% in 1994 (Figure 4). To understand this trend a brief historical review is needed.

Figure 4: Aggregated Sales to R&D Ratio (%)



Source: (H. Grabowski, Vernon, & DiMasi, 2002)

In the 1960s and 1970s some studies found diminishing returns to R&D compared with the pre-war period. The pre-war period had experienced a wave of new breakthrough drug introductions, including new antibiotics, new treatments for hypertension and new classes of antidepressants to mention a few. Instead of focusing R&D efforts on new therapeutics areas, pharmaceuticals invested in developing drugs that showed superiority to established drugs. By the 1960s this approach was not only costly but also unprofitable and the industry entered period of technological maturity.

To overcome the diminishing return, by the early 1970s pharmaceuticals began to focus their R&D investment on new therapeutics areas, with a new approach known as the "rational drug-design" – an approach with a more focused screening of new compounds. An important milestone came with SmithKline's ulcer drug, Tagamet, which validated this new approach. Within just a few

years it became the world's best-selling drug (H. Grabowski et al., 2002). Appendix 1: Important Drug Milestones shows some of the more important milestone product launches since the 1970s.

The change in R&D strategy is captured in what has been labelled as the "virtuous rent seeking model" of R&D competition in the pharmaceutical industry, first mentioned by Scherer (2001). In this framework, pharmaceuticals compete (through investment in R&D) in the search for new therapeutic compounds that yield an above-average expected return. This is in line with indication regarding first-mover advantages (Lieberman et al., 1988), where empirically the first mover in a new therapeutic class takes between 40 to 60% of the market, and the second only around 15% (Gassmann, Reepmeyer, & Zedtwitz, 2008). Coming third is no longer profitable. This strategy however produced a rapid increase in the industry R&D expenditure, escalating after the end of the 1970s (Figure 4). Three decades after the launch of Tagamet, the innovation today still reflects the focus on investment in higher return products with increased R&D intensity as a consequence.

There are many moving parts associated with the increase in the R&D intensity, and more rigorous analysis is required to assess the trend of rapidly growing R&D costs. One explanation is the intense rivalry in the patent-race as mentioned above. According to a study from DiMasi & Faden (2009), 90% of all first-in-class medicines being approved already had a potential competitor in at least phase II clinical testing. This is a significant increase since the 1970s when that number was 23%[5]. Intense rivalry was further reflected in the time a medicine was the only drug available in its therapeutic class. The number of years has declined from a median of more than 10 years in the 1970s to below 2 years by 1998[6].

2.4.2. Analyzing the Drug Development

The most important reasons for higher R&D costs can be summarized as follows: 1) the cost of resources invested in drugs that fail at some point during the development process; 2) average development times; 3) out-of-pocket preclinical and clinical costs; and 4) and the cost of capital (DiMasi & Grabowski, 2012).

[5] See Figure 28 in Appendix 4: Figures for the Pharmaceutical Industry Analysis for illustration.

[6] See Figure 29 in Appendix 4: Figures for the Pharmaceutical Industry Analysis for illustration.

Development times become costly, as the capitalized cost estimates grow proportionally with the increase in development times, everything else being equal. Since the mid-1960s, there has been a general increase in time it takes to develop a drug from 2.8 years in the mid-1960s to more than 6.2 years in the 1990s. Though experiencing in small decrease in the 2000s, new studies have shown that the average time to develop a new medicine has increased to 6.7 years[7]. (Gassmann et al., 2008; Tufts (CSDD), 2014). DiMasi, Hansen, & Grabowski (2003) estimated the increase in development times between 1970s to the 1990s increased the average costs of developing a drug by 24%. Developing a drug today takes approximately 10 years from drug discovery to final FDA approval including pre-clinical studies.

Technical or development risks in drug developments also seem to be worsened over time adding yet another explanatory factor for the increase in overall R&D costs. DiMasi et al. (2003) found the clinical success rate of 21.5% in a sample comprising investigational drugs that entered clinical testing between 1983 and 1994. In a more recent study by Tufts CSDD (2014), showed the success rate for substances entered clinical testing between 1995 to 2007 has decreased significantly to 12%[8].

Opportunity costs, however account for a far greater proportion of the increases in R&D costs. Since drug developments include huge investments and a significant time lag before revenues can be earned, time costs of money is high. Four separate survey-based studies with samples spanning from 1970 to 2010 gathered from the work of (DiMasi et al., 2003; DiMasi, Hansen, Grabowski, & Lasagna, 1991; R. W. Hansen, 1979) and including the recent study from Tufts (CSDD) (2014) all tried to capture the out-of-pocket outlays to average drug development, including the capitalization of these outlays to the point of marketing approval with an appropriated discount rate to capture the time cost of money. The studies demonstrated a significant R&D costs increase, reflecting the dramatic industry change following the enactment of the 1962 Amendments to the Food and Drug Cosmetic Act of 1938[9]. Figure 5 shows the increase in preclinical, clinical, and total preapproval average capitalized costs. The total average developing costs including cost of failure rose from

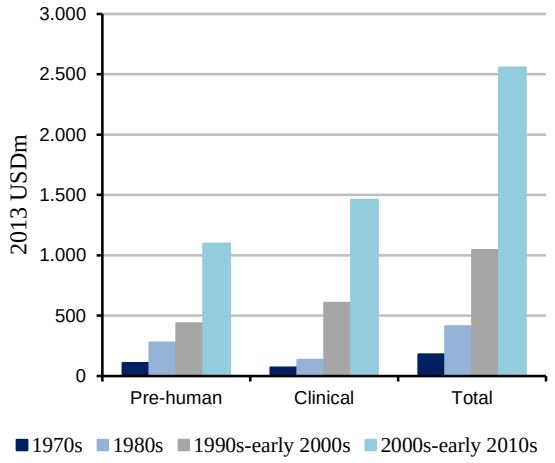
[7] See Figure 30 in Appendix 4: Figures for the Pharmaceutical Industry Analysis for illustration.

[8] See Figure 31 in Appendix 4: Figures for the Pharmaceutical Industry Analysis for illustration of clinical phase transitory probabilities and the overall clinical approval success rate from substances entering clinical trials between 1995 and 2007.

[9] See Appendix 2: FDA Regulation and an Overview of the R&D Process for a description of various government enactment involving the pharmaceutical industry

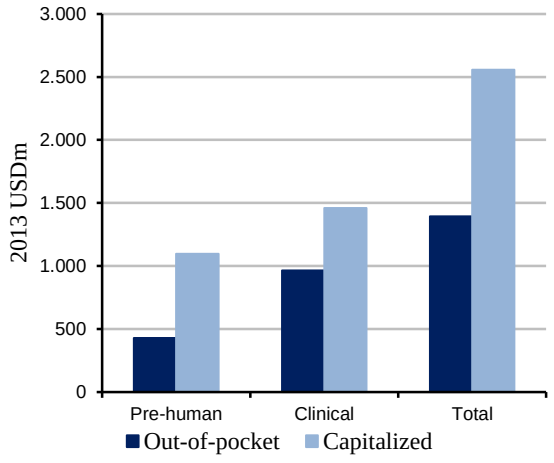
USD179m in the 1970s to USD2.6bn in the early 2010s. Figure 6 shows the out-of-pocket costs versus the costs capitalized, where the time costs represent 45% of the total costs. This is a decrease of 5%-point compared to the sample from the 1990s.

Figure 5: Growth in Capitalized R&D Costs by Approved Drug



Source: (DiMasi et al., 2003, 1991; R. W. Hansen, 1979; Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2014)

Figure 6: Out-of-Pocket and Capitalized Cost per Approved Drug (2010)



Source: (Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2014)

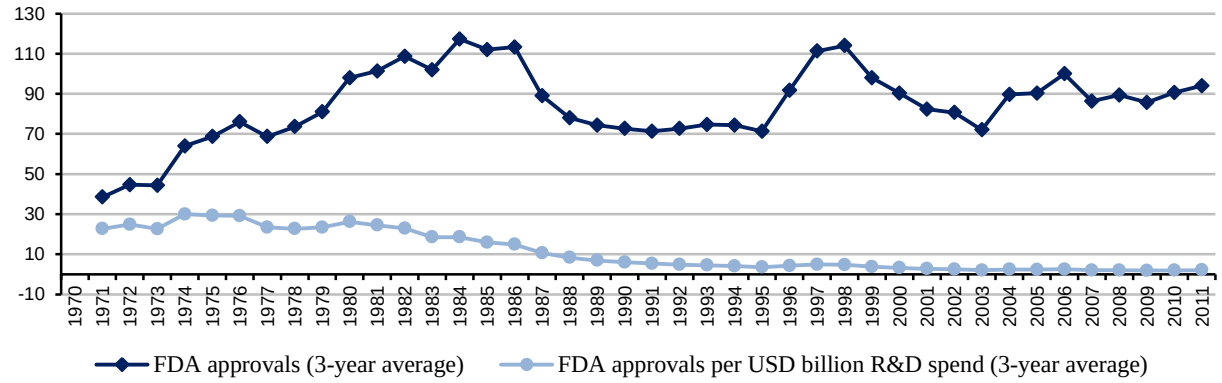
Increases in cash outlays used in clinical phases and higher drug failure rates during clinical testing are the biggest contributors to increases in R&D costs, where development time and cost of capital had only a modest effects (Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2014).

With the high R&D intensity one should expect an equivalent expansion in the R&D output. R&D output however, as measured in the number of patents obtained, shows a more disappointing development.

2.4.3. Decreasing Productivity as Measured in Patents

Looking at the R&D output back the 1970s, the number of approved drugs, formulations and indications has more than doubled, but when comparing the output with R&D spend over the same period, the number of approvals per USD1bn spent on R&D has reduced by a factor of 15 (Figure 7) (OECD, 2015).

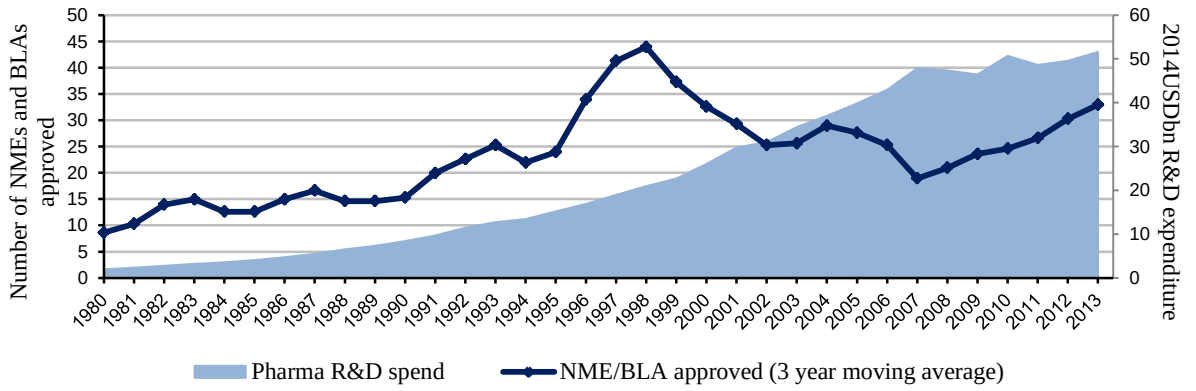
Figure 7: Annual FDA Pharmaceutical Approvals, per USD Billion R&D Spend (indexed to 2008 USD)



Source: (OECD, 2015)

This gap between input and output becomes even more evident when comparing the growth in R&D expenditure and the numbers of US small molecules and biologics approvals over a long period of time (Figure 8). Analysts have even divided the industry into an "Era of Abundance" (pre-2005) and an "Era of Scarcity" (post-2005), reflecting the drop in R&D productivity of 70% as measured by fifth year product sales per billion dollar R&D expenditure in recent years (Thomas Reuters, 2015).

Figure 8: New Drug and Biologics Approvals (LHS) and R&D Spending (RHS)



Source: (Pharmaceutical Research and Manufacturers of America (PhRMA), 2015; U.S. Food and Drug Administration, n.d.-a)

So how has the R&D cost performed when analyzing the economic return? The accounting return for pharmaceutical companies appears high compared with other industries, leading many to speculate that the pharmaceutical industry is characterized by a monopoly and high economic rent with high barriers to entry arising from regulation, high R&D expenditure, and promotion to protect it (DiMasi & Grabowski, 2012). The literature consists of several approaches to explain the higher

returns. This paper uses approaches that are more in line with financial literature that connects above-average riskiness of investments with higher expected returns.

2.4.4. Diminishing Productivity as Measured in Economic Return

The pioneer study that analyzed the industry's economic return to its appropriate cost of capital was the study conducted by H. Grabowski & Vernon (1990). With new drug approvals introduced in the 1970s they analyzed the internal rate of return and the present value of sales generated. Subsequent studies from H. G. Grabowski & Vernon (1994) and H. Grabowski et al. (2002) used similar methodology, so that the development of the net economic returns of new drug introductions from 1970 through 1990s can be compared.

The studies revealed an increasing trend in the mean industry returns from the 1970s to the mid-1990s (Table 2). However, when comparing it with the corresponding cost of capital, then the economic returns are only in modest excess of the opportunity costs. In addition net economic return is showing a negative trend.

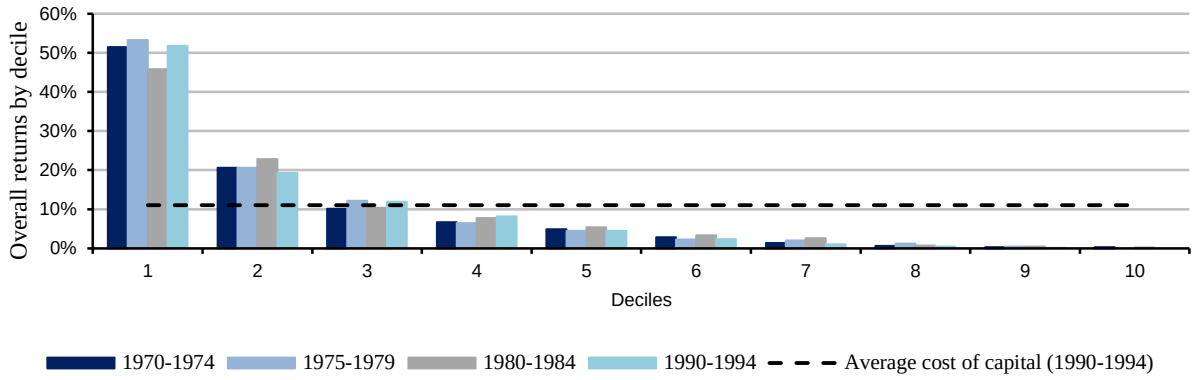
Table 2 :Mean Returns and Cost of Capital for Different Time Cohorts

Year	Mean IRR	Cost of capital	Net economic return
1970–1974	7.0%	9.0%	-2.0%
1975–1979	9.7%	9.0%	0.7%
1980–1984	11.1%	10.5%	0.6%
1990–1994	11.5%	11.0%	0.5%

Source: (H. G. Grabowski & Vernon, 1994; H. Grabowski et al., 2002; H. Grabowski & Vernon, 1990)

The studies further showed that the revenue distribution is highly skewed, as shown in Figure 9 reflecting far greater revenue generation from the top decile compounds in all sample cohorts. It further display the average cost of capital for the 1990-1994 cohort, and reveal that the only the top three decile have present values in excess of their cost of capital. Thus, the funding of a company's pipeline depends on a few current products.

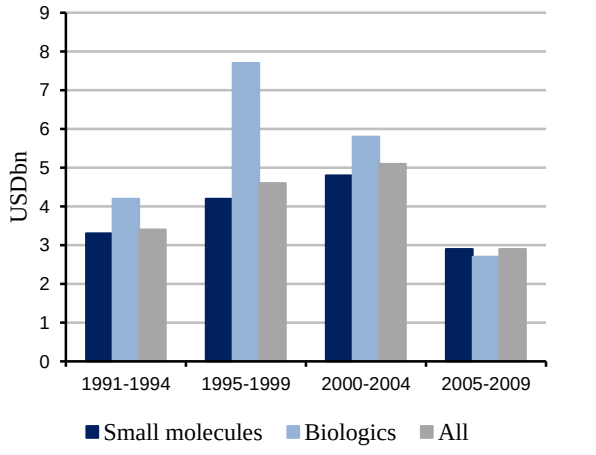
Figure 9: Present Values of Four Sample Cohorts of New Drug Introductions Accounted for by Decile.



Source: (H. Grabowski et al., 2002)

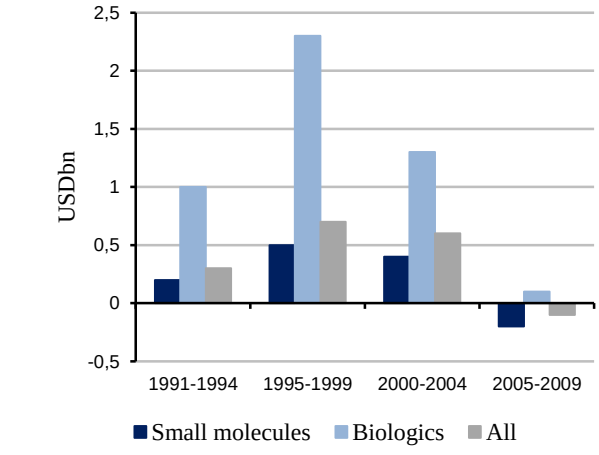
(Berndt et al., 2015) investigated the average present value of life time global net sales of small molecules and biologics with a more present sample. They showed that there appears to be a more positive trend, at least from the 1991-1994 to the 1995-1999 sample, which then change to a negative trend going forward. Newly launched prescription drugs (excluding generic drugs) between 2005 and 2009 only had an average net present value of global sales of USD2.9bn (Figure 10). When comparing this to the still increasing average development costs, the average lifetime net economic return was even slightly negative (Figure 11).

Figure 10: Average present value of lifetime global net sales of prescription drugs



Source: (Berndt et al., 2015)

Figure 11: Average lifetime after-tax net economic returns of prescription drugs



Source: (Berndt et al., 2015)

2.4.5. Main Indication of Diminishing Return

As indicated earlier, there are many moving parts to the declining economic return both from the supply side and the demand side, and from political movements as well (often sending shocks through both the supply and the demand side).

Where the political initiatives expanded the pharmaceutical patient reach in the 1960 and 1970s, today political action aims to bring medical costs down by increasing the supply side. Many scholars have argued that the regulatory initiatives harm the innovation incentives for pharmaceuticals. For instance, Peltzman (1975) in a sample from 1948-1974 found that the annual new drug introductions flow fell 66% after the enactment of the 1962 Amendments[10], where the average cost of a new compound increased by a factor of 1.9 (H. G. Grabowski, Vernon, & Thomas, 1978). Furthermore, Thomas (1990) found the US total development times increased from 35 months in 1960 to 145 months in 1980 after the 1962 Amendments.

This paper focus on how increased competition has affected the economic returns in the industry. Since the emergence – and rapidly growing sales – of generic products, there has been an increasing threat to established pharmaceutical companies' business models, as their blockbuster products run out of patents (Gassmann et al., 2008). An increasing risk for the virtuous rent seeking pharmaceuticals is the heavy reliance on only a few high–volume products to fund future pipeline products[11].

2.4.5.1. Generic Competition

Prior to 1984 generic competition was close to non-existent, but with the enactment of Hatch-Waxman Act in 1984 generic drugs have since then grown rapidly. Today nearly 9 out of 10 US prescriptions are filed with generics, and in 2014, the generic industry generated USD74.3 billion in sales, equivalent to 10% of the global sales. Additionally, the generic market is growing at faster pace than the branded drug market, steadily increasing its share of the total market [12] (EvaluatePharma, 2015; PhRMA, 2015).

[10] See Appendix 2: FDA Regulation and an Overview of the R&D Process for regulatory enactments in the pharmaceutical industry

[11] See Appendix 3: Block Buster Imperative Strategy for a brief description of the Blockbuster Imperative Strategy and to why this strategy is sensitive to increased competition.

[12] See Figure 32 and Figure 33 in Appendix 4: Figures for the Pharmaceutical Industry Analysis for illustrations.

The main result from the Act was the creation of a system where branded product sales were generated almost entirely during the market exclusivity period with generic counterparts replacing market share of the original drug immediately after generic entry (H. Grabowski, Long, & Mortimer, 2013). However, generic competition did not come without consequences. According to (H. Grabowski et al., 2013), the average length of exclusivity for all NMEs between 2011 and 2012 was 12.9 years by year of first generic entry, compared to 13.5 years in the period 1995-1996 (Figure 12).

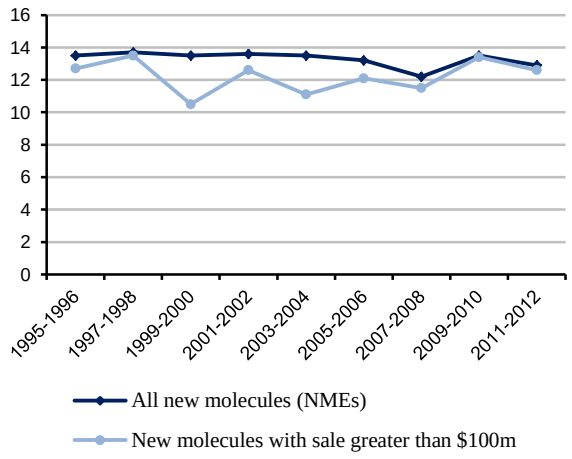
In addition, the number of generic entrants is higher for drugs with larger sales before the first generic entry – a trend that has been increasing over time. E.g. blockbuster drugs generating more than USD1bn in annual sales between 2009 and 2011 experienced on average 9.5 generic equivalent entrants within 12 months of the loss of patent exclusivity. That number was 6.0 on average between 1995 and 1998. In addition, the average market exclusivity period for these billion dollar products were even shorter, i.e. the average market exclusivity period of billion dollar products between 2002 and 2005 was only 11.2 years (H. G. Grabowski & Kyle, 2007).

Furthermore, an analysis from the Congressional Budget office (US Congress Congressional Budget Office (CBO), 1998) estimated that the average returns from marketing a new drug was reduced by 12% in the first decade after the Hatch-Waxman Act was enacted. The CBO report concluded that the negative effects on returns from generic market erosion were far greater than gains obtained from patent extensions.

Paragraph IV challenges[13] have increased significantly over the past 10-15 years. In 2012 81% of drugs experienced a Paragraph IV challenge compared with only 9% of drugs in 1995. Furthermore, the generic challenges occur much sooner. The average time between a new product launch and a Paragraph IV challenge was 18.7 years in 1995. That time fell to 6.9 years in 2012 (Figure 13).

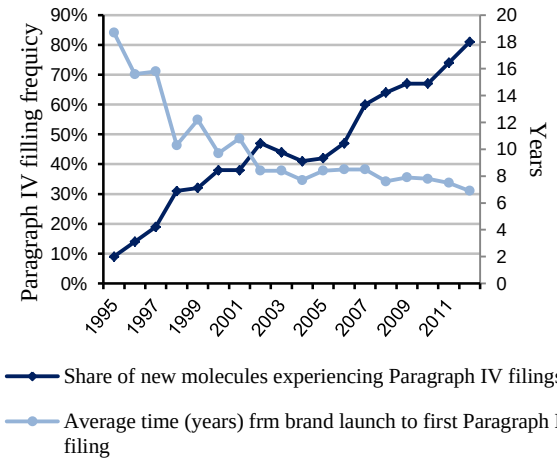
[13] In short a Paragraph IV challenge, allow generic companies to "challenge" branded product before they expired. See Appendix 2: FDA Regulation and an Overview of the R&D Process for more information on Paragraph IV challenges.

Figure 12: Average Market Exclusivity Period (in Years) by Year of First Generic Entry



Source: (H. Grabowski et al., 2013)

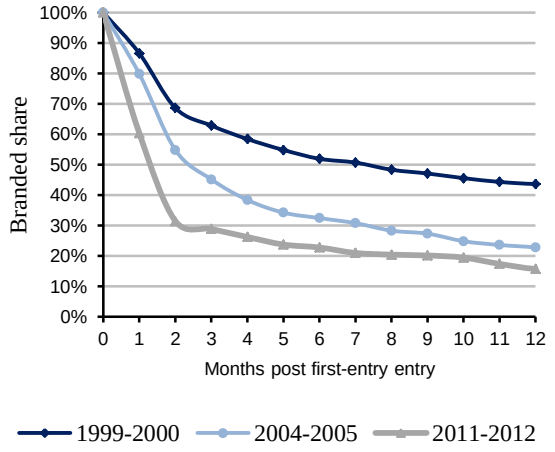
Figure 13: Paragraph IV filing frequency (LHS) and timing (3-year moving average) (RHS)



Source: (H. Grabowski et al., 2013)

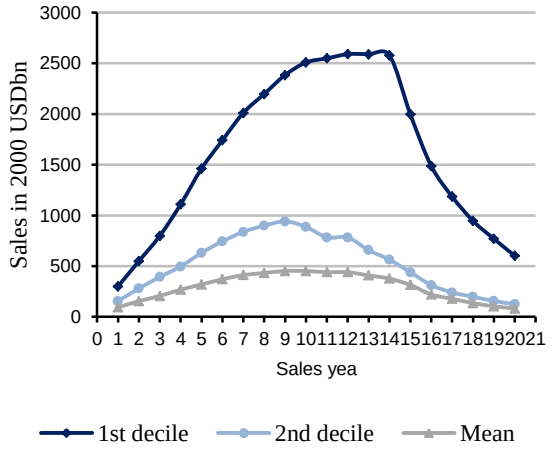
Market share erosion for branded drugs after patent expiry has also experienced a dramatic fall. For instance branded drugs in 2012 saw their market share drop by almost 85% on average 12 months after its first year of generic entry compared to a generic market erosion of 55% in 1999 (Figure 14). Furthermore, market share erosion hits harder for branded drugs selling for more than USD1bn annually (H. G. Grabowski & Kyle, 2007), as displayed by H. Grabowski et al. (2002) in Figure 15. Top decile drugs experience a much severe drop in sales at patent expiry compared with the second decile and the mean.

Figure 14: Average Month Branded Product Share of Total Market Following Generic Entry



Source: (H. Grabowski et al., 2013)

Figure 15: Worldwide Sales Profiles of 1990 to 1994 New Drug Introductions.



Source: (H. Grabowski et al., 2002)

Although the average lifetime of a drug has not declined by more than 6 months over the period it shows a general declining trend, where blockbuster drugs are hit harder. Additionally, this declining trend is most likely enhanced by generic manufacturers challenging the patents protecting the brand more often and earlier in the branded drug's life cycle.

In conclusion, since significant share of revenue is attributed to only a few blockbuster drugs the companies expose themselves to a great amount of undiversified risk. Further, these risks have increased over time in line with a declining R&D productivity - both in terms of R&D output and economic returns, and increased generic competition, and consequently weaker patent protections.

The above analysis showed that the pharmaceutical industry has gone through some interested changes and therefore serves as a suitable empirical context to answer the overall research question.

3. Theoretical Framework

As indicated in the introduction this study seeks to investigate the overall expected firm performance related to new product innovations, and how that performance is influenced by competition. It is therefore essential to evaluate the performance of a given innovation on a higher level than on the product itself. For instance the work carried out by (H. G. Grabowski & Vernon, 1994; H. Grabowski et al., 2002; H. Grabowski & Vernon, 1990) in the Pharmaceutical Industry

Analysis evaluated product performance based on the net present value on a product level only. They did not show how the individual products might influence the expected performance of the firm as a whole. This is often the case for most empirical evidence evaluating new product innovation (Sharma & Lacey, 2004). A reasonable explanation for this is that the evaluation of product performance is clean of any confounding event that might influence the estimated performances. This becomes a relevant issue when evaluating overall firm performance related to a single innovation. However, some methods can be applied to overcome "noisy" estimates.

In general it is a delicate task to assess and value financial impact of specific product development activities and to obtain unbiased estimates of expected future cash flows attributed to a new product. These estimates cannot be collected objectively. Different agents assign different assumptions to future prospects. One solution to maximize the "objectiveness" in estimations is to rely on market assessments as reflected in changes in stock prices as a reaction to a specific event of interest (Brown & Warner, 1980). Hence, one could rely on the market's assessment of a new product as measured by the changes in stock prices at the moment the product is introduced. This correlation between expectation of firm performance, as reflected in the stock price and product innovation consequently becomes an empirical question under the theory of the efficiency market hypothesis (EMH).

3.1. The Efficient Market Hypothesis

Usually, scholars divide market efficiency into different forms depending on predefined assumptions of the market. The extreme version of market efficiency states that security prices fully reflect all available information. A predefined assumption for this strong statement is that all information and trading costs are zero. In reality positive information and trading costs are present, so the strong version of EMH is by definition false. A weaker version of the EMH[14] says that prices reflect all information up until the point where marginal benefits of acting on information is no longer in excess of marginal costs (E. F. Fama, 1991). Therefore, prices will change whenever there are profits to be made.

The EMH, at least in the semi-strong form, is widely accepted in finance literature by now, and many researchers support the hypothesis stating that stock prices reflect all publicly available information and that prices adjust efficiently to new firm-specific information. The cleanest

[14] (E. F. Fama, 1991) defines market efficiency tests in the semi strong form as event studies.

evidence on market-efficiency comes from event studies[15] especially event studies relying on daily stock returns (E. F. Fama, 1991). Subsequent empirical literature providing evidence in favor of the semi-strong version of the EMH is rich in a variety of financial areas such as dividend (E. Fama, Fisher, Jensen, & Roll, 1969)[16], and earnings announcements (Rendleman, Jones, & Latané, 1982), and stock splits (Reilly & Drzycimski, 1981).

Applying the same approach to product innovation and by assuming the EMH in a weaker form, new information about product innovation should be reflected in the security prices as soon as this new information becomes available. Hence, by relying on the EMH, it is possible to assess the expected firm performance related to product innovation, as summarized in the stock price, by isolating the impact from product innovation reflected in the security prices.

Supposedly the issue about collecting unbiased estimates for firm performance is solved by relying on the average valuation of many actors in the market. However, the market efficiency is not testable alone. It must be tested jointly with a model of market equilibrium (E. F. Fama, 1991). As seen in the Event Study Methodology section a precondition for applying event studies and to test market efficiencies is to define an equilibrium model in order to estimate abnormal returns. But in event studies, estimations are seldom sensitive to changes in equilibrium models (Peterson, 1989) – especially when comparing it to how model changes influence product evaluation on a product level. For instance, in the work of (H. Grabowski et al., 2002) as shown in the industry analysis, only 3 out of 10 drugs earned returns in excess of their development costs. In this framework they applied the Capital Asset Pricing Model (CAPM) to calculate the cost of capital. However, in more recent study, they calculated a cost of capital on the basis of the Fama-French Three-Factor model and applied on the same raw data as their previous study. However, the cost of capital was now 14.36% compared to 11.02% in the CAPM framework, significantly reducing the present value of drug approvals. Consequently, with the Fama-French framework only 2 out of 10 drug approvals have a positive net present value (DiMasi, Vernon, & Golec, 2010). Estimations on individual product innovations on a product level might be highly influenced on the basis of the researchers' predefined assumptions.

Thus, the most unbiased estimations are collected by estimating expected firm performance by assuming the semi-strong-form (or event studies) of EMH holds. Furthermore, because these tests come closest to avoid the joint hypothesis problem, event studies provide the most direct evidence

[15] A deeper discussion on event studies is carried out under Event Study Methodology.

[16] The ever event study was carried out by (E. Fama et al., 1969).

on market efficiency (E. F. Fama, 1991), and hence the most cleanest estimates of expected firm performance.

3.2. Pharmaceutical Industry as Research Context

To collect the expected firm performance estimates related to new innovation, one needs data that satisfies certain conditions crucial to the event study methodology. In this study the pharmaceutical industry serves as an approximation to collect expected firm performances for the entire product market. The pharmaceutical industry was selected for several reasons. First, the industry as a research context provides the necessary conditions to apply an event study methodology. The outcome of a drug approval is clearly evident, as the FDA serves as gatekeeper for the North American pharmaceutical market [17]. Without an approval by the agency, pharmaceutical companies are prohibited to sell their product in the US (U.S. Food and Drug Administration, n.d.-a). The FDA's final approval is then a clearly marked event that can be precisely pinpointed to each product application. The approvals thus represent new information related to product innovation that is then valued on the basis of changes in security prices for a given firm once information about the approval becomes available to the market. Approvals – or the expected firm performance obtained at that particular day, are thus an approximation for the value of innovations on the overall expected firm performance. Alternatively, the expected firm performance can be interpreted as the economic incentives for the firm to innovate.

To understand the last part and to make sense out of why expected firm performance can be collected through a test of the EMH, it is important to make a clear interpretation of the economic incentives for shareholders. As the expected firm performance in relation to new innovation is implicit a measure of how the market perceive a given innovation, shareholders react to new innovation if and only if new innovation changes the fundamental value of a given firm. This statement rests heavily on the Principle of the Conservation of Values which says that corporate initiatives that do not increase future cash flow do not increase value. Hence, if new innovation increases fundamentals of a firm, shareholder reward that firm by increasing its firm value and vice versa. The economic incentives for shareholders stem from the promise of increased future earnings related to new innovation brought to the market by the firm. This in turns provides economic

[17] For a brief description of the Food and Drug Administration's (FDA) regulatory process and an overview of the R&D process, see Appendix 2: FDA Regulation and an Overview of the R&D Process.

incentives for firms to innovate as long as the incremental earnings from innovative are positive. The economic incentives for the firm to innovate thus become a continuous and accelerating cyclical process at least as long as the incremental profit from innovating is positive.

3.3. Empirical Evidence of FDA Approvals and Firm Performance

The literature for market responses to FDA approval announcements is relatively scarce. Prior literatures are implicitly testing EMH whenever the agency approves or rejects a product, failing to investigate changes to valuation effects over time or to give any reasonable explanations to why that might be case.

One of the pioneer studies, conducted by Bosch & Lee (1994) investigated the valuation effect of FDA product approvals, rejections and disciplinary decisions on firms that operate in the food and drug industry with decisions collected from 1962 through 1989. They revealed a significant wealth effect on FDA decisions on firms associated with approval and rejection decisions. Additionally, they discovered that significant price changes were present almost up to the announcement day, suggesting a huge amount of uncertainty were still present at the final decision, despite a continuous flow of information delivered to the market through the entire decision process.

In a more recent study, Sarkar & de Jong (2006) investigated the announcement effects at four points in the FDA review process and explored conditions that can affect final approval from data collected from 1990 to 2001 (on a product level only). In their research they concluded that investors reacted positively to positive signals from the FDA and negatively to rejection indicators, which is not surprising given previous studies. However, in contrast to Bosch & Lee (1994) they found that the final approval resolved only a small degree of uncertainty, which was validated by a higher abnormal return associated with the initial approval letter by the FDA. Additionally, they found the magnitude of positive reactions to marketing approvals to be less than reactions found in the earlier work of Bosch & Lee (1994)

In two separate studies Sharma & Lacey (2004, 2007) showed that drugs rejected by the FDA produce a far greater financial loss than gains attributable to drug approvals, even when isolating the most path-breaking product approvals. (Ahmed, Gardella, & Nanda, 2002) showed that shareholder wealth losses from drug withdrawals often exceed the out-of-pocket expenses resulting from the withdrawal.

3.4. Connecting Economic Incentives to Competitive Implications

The theoretical framework in this study is built upon the U-shaped relationship between product market competition and the incentives to innovate, as set up by Aghion et al. (2005). Hence, this study allows for a pre-innovation rent by the incumbent firms in the framework, and they can respond without limitation to competition from both potential entrants and among established firms within the industry. In addition all innovations by leaders and followers occur step-by-step.

3.5. Hypotheses

Several important indications emerge from the industry analysis and the empirical research about market responses to FDA announcements conducted so far. Firstly, public information about new product development approvals and rejections is impounded somewhat efficiently into the stock price, as studies have shown that investors reward the sponsoring firm financially when a drug is approved and punish them when the sponsoring firm is unable to deliver. The market seems to have become more efficient in recent times, as Sarkar & de Jong (2006) showed that the share price performance in terms of rejection was spread over only 1 day, compared to information leaks spread over 5 days in in the older study conducted by Bosch & Lee (1994). This paper does not question the efficiency of the market when it comes to product approvals, as previous research papers have already successfully supported the EMH, at least in the semi-strong form (Sarkar & de Jong, 2006; Sharma & Lacey, 2004). Although taken this assumption as given, the findings in the Event Study Analysis are implicitly being tested for market efficiencies. A pre-condition to use the expected firm performance in relation to product innovation as an approximation to the economic incentives for firms to innovate, is that the EMH holds in the semi-strong form.

Secondly, it appears that firm performance relating to product successes and failures are largely asymmetric. Sharma & Lacey (2004) showed that there is a significant difference between shareholder wealth effect when comparing firm performance to product successes and failures. The current research question limits the study to focus on product approvals only. However, the presumably large loss from failures might have managerial implications when managers evaluate investment opportunities – managerial implications are discussed in Managerial Implications section.

Thirdly, the pharmaceutical industry itself has gone through some significant changes which can be attributed to competitive implications. The industry thus creates a suitable framework to investigate the current research question.

This study will add to the current literature about economic incentives related to new innovations using the pharmaceutical industry as an approximation. Economic incentives are measured as the magnitude in expected firm performance as respond to product development efforts here in forms of new drug approvals. Further, the study is set up to investigate how competitive forces might influence these economic incentives. The current study distinguishes itself from prior research in two ways. First, prior research linking product innovation, incentives and competition fails to the show if product innovation has financial implications beyond the product itself. Furthermore, literature connecting expected firm performance related to product innovation fails to show implication beyond the "simple" test of EMH.

To be able to answer the research question efficiently the question is transformed into two hypotheses that can be tested. The following section explains how the hypotheses are derived through two forms of implications: industry and managerial implications, which effectively work together.

3.5.1. Industry Implications

As indicated in the Pharmaceutical Industry Analysis section prior to the Hatch-Waxman Act in 1984 the pharmaceutical industry was characterized by a monopoly-like environment. Few large companies dominated the market, low but increasing development costs, no real threat from generic competition, monopoly-like conditions in terms of longer market exclusivity periods, and high-value potential in pipeline portfolios were among the factors that earned the industry above--average returns. These returns draw parallel to what competing theories define as monopoly rents or entrepreneurial rents. By introducing new innovations, here in the form of new drug introductions, and obtain a small monopoly through the lifetime of the patent received, the pharmaceuticals have the ability to earn an above-average return. These rents were further protected by long market exclusivity periods obtained at the drugs' approvals as suggested by (Aghion et al., 2012). In addition, incumbent firms competed with products close to the technology frontier – an environment Aghion et al. (2005) define as a "neck-and-neck" sector, where incumbents firms are operating at similar technology levels.

Naturally, such an environment attracts competition, but competition, at least from generic imitations, were kept at bay due to regulatory reasons[18].

With the Hatch-Waxman Act in 1984 the pharmaceutical industry was abruptly exposed to a swarm of generic imitation. The interesting question here in relation to focus of this paper: How did the increase in competition affect the economic incentives to innovate?

Adopting the framework from Aghion et al. (2005), one can expect a positive reaction on innovation output from increased generic competition once allowing pre-innovation rent into the model. To "escape competition" incumbent firms have the incentives to invest heavily in R&D as competition increases the incremental profits from innovation. Further, to balance the provisions for generic competition, the government allowed additional patent extension through a patent term restoration – i.e. post-innovation rent got even more protected. Hence, increased competition is expected to decrease the pre-innovation rents by more than it decreases the post-innovation rents keeping the net innovation somewhat stable – or maybe even increasing as longer market exclusivity periods protected the post innovation rent even further.

This approach is directly transferred to the economic incentives for firms to innovate. As competition increases, from a relatively low initial level of competition, the value of innovation as measured in the expected firm performance is expected to increase. The intuition is that greater competition in these neck-and-neck environments increases the incremental earnings from innovating for the incumbent firm at the expense of economic disincentives for laggard companies to innovate. Hence, the "escaping competition" is dominating in this situation. Furthermore, all else being equal, increased future earnings from new innovation must increase the fundamental value of a given firm[19]. These fundamental changes must be materialized in the firms' stock prices – i.e. the expected firm performance. The last part stems from the economic incentives for shareholders to inject capital in to company to enjoy the economic gains from new innovation. Hence, the economic incentives for firms to innovate become a self-perpetuating effect.

[18] Prior to the Hatch-Waxman Act generic equivalents to the original branded drug had to undergo same time consuming and costly regulatory procedure as the branded version. See Appendix 2: FDA Regulation and an Overview of the R&D Process.

[19] This statement relies on Principle of the Conservation of values, which basically implies that any activities by a firm that does not increase future cash flows does not create any value (Koller et al., 2010).

3.5.2. Managerial Implications

Inspired the work of Machlup (1967) and Hart (1983), managers automatically have the incentives to respond when their firms are introduced to competition. Due to the ownership separation, managers have the opportunity to exercise discretions that are not in the best interest of the firm – i.e. the classic principal-agent problem. But when competition jeopardizes the managers' own long-term income, the best interests for both the manager and the firm reconcile as competition becomes more efficient.

In addition, the presumed asymmetrically large loss from failing a product innovation as reported by Sharma & Lacey (2004) and Ahmed et al. (2002), ensure that executives have factored in a substantial risk premium when considering new development projects that require commitment of large sums of money. Hence, it is assumed that management only engage in new development projects when they are almost certain that projects are profit maximizing for the firm.

The managerial implications work as a reaction to the industrial implication. The assumption is that executives are not watching passively when competitive forces interact with their own self-interest. Hence, when executives are exposed to competition, they have the economic incentives to innovate as the firm's interest of profit maximization unifies with the managers' own income maximization. The managerial implications simply connect the economic incentives for firms to innovate when competition increases, , to the manager's incentives to maximize firm value when competition jeopardizes his long-term income.

Thus, to evaluate the economic incentives for the firm to innovate and how competition might influence these incentives it is hypothesized that:

H1: The economic incentives for the firm to innovate are an increasing function of competition.

Further, the economic incentive for firms to innovate is expected increase at a steeper rate in environments with low initial level of competition.

However, at some point along the curve as competition increases, the incremental earnings from innovation become less clear. When a certain threshold is met the pre-innovation rent becomes equal to zero. At this point the incremental profit from innovating becomes negative, which discourages incumbent firms to innovate and the escaping competition effect cease to exist. From

here on out, most innovations are made from new entrants with low initial profits exploiting the post-innovation rents. As more entrants squeeze out the post-innovation rent, the further competing products in the industry move away from the technology frontier, and the Schumpeterian effects becomes a snowball effect in line with intensified competition.

Intuitively, when incremental earnings from innovation turn negative, additional innovation at this point destroys value. Instead of shareholders rewarding new innovation by increasing firm value, in theory when future earnings contribute negatively to fundamental values, shareholders will punish innovation. According to on Principle of the Conservation of values, innovation that destroys value must be reflected negatively in the expected firm performance. This turns the incentive to innovate into a disincentive for incumbent firms to innovate, which then leaves all innovation to potential entrants with low initial profits further exploiting the post-innovation rents.

In addition, as a consequence of increased competition, the technology advantages in terms of patents protecting the post-innovation rents are expected to become under pressure. As shown in the Pharmaceutical Industry Analysis section, the market exclusivity period was reduced by the entrance of generic competition. Hence, the negative effect from competition becomes even stronger once the incremental profits for the incumbent firms to innovate become negative.

Thus, as an extension to the *H1* it is hypothesized that:

H2: The economic incentives for the firm to innovate become a decreasing function of competition once a certain threshold is met.

If the null is rejected in both *H1* and *H2*, the correlation between the economic incentives to innovate for the firm and competition follows a U-shaped relationship as indicated by Aghion et al. (2005).

4. Methodology

To test the two main hypotheses set up in the Theoretical Framework section, two methods are applied – event study methodology and a regression analysis. In the Methodology section the applications for two methods are discussed.

4.1. Event Study Methodology

The event study methodology is applied for three crucial reasons. One, as indicated in the Theoretical Framework section event studies provide the cleanest test of the EMH especially when the event study relies on daily stock returns. Consequently, if the weaker form of the EMH holds the study obtains the most unbiased estimations of the expected firm performance as measured in the abnormal returns. In addition, the study will provide a valid approximation of economic incentives for firms to innovate as defined under Theoretical Framework.

Second, the event study itself will give an indication of how the economic incentives have developed the last 30 years. The analysis however cannot explain what might be the underlying causes for these changes. Nonetheless the study will show if any systematic changes in the abnormal return are present, which gives a valid reason to investigate how competition might influence the economic innovation incentives.

Third, the event study provides the necessary data to analyze how the competitive implication may influence the economic incentive to innovate – an investigation that can be carried out by the regression analysis. Hence, the two methods need to work together to give a sufficient answer to the overall research question.

In general an event study measures the effect of an economic event on the value of a firm using data collected from the financial market (MacKinlay, 1997). Event studies are thus, as indicated earlier, a direct test of market efficiency hypothesis. With unanticipated events, the magnitude of the abnormal return at the time of the event should then be the true value reflected on the wealth of the firms' shareholders (Brown & Warner, 1980). In relation to the current study, then the abnormal returns at the time of an event (drug approval) reflect the true value of a firm's innovative efforts and should be reflected in a firm's stock price (expected firm performance). Hence, the abnormal return reflects the expected firm performance after a new innovation has been introduced to the market.

To determine the impact of an event a model is required to measure the abnormal return. Theoretically, the abnormal return is the actual ex post return of the security over the event window subtracted by the normal return of the firm over the event window. The normal return is defined as the expected return without conditioning on the event taking place. Thus, for firm i and event day t the abnormal return is

$$AR_{it} = R_{it} - R(R_{it}|X_t) \qquad (1)$$

where AR_{it}, R_{it} and $R(R_{it}|X_t)$ are the abnormal, actual and normal return, respectively for time period t. Several models can be used to calculate the normal return of a given security, and they can be categorized into two groups – statistical models and economic models. Brown & Warner (1980) and MacKinlay (1997) identify several common models. In this study only those applied are discussed here:

- Market Model

The market model (as all statistical models) relies on statistical assumptions concerning the behavior of asset returns and do not take any economic arguments into account. The general assumption for this model is that asset returns are jointly multivariate normal, while they are independently and identically distributed through time. Thus, calculating the coefficients for the market model over the estimation period of x-amount of days prior to the event, allow one to predict the stock behavior around the event date. The market model relates the return of any given security to the return of the market portfolio. For any security *i* the market model is:

$$R_{it} = \alpha_i + \beta_i R_{mt} + \varepsilon_{it} \qquad (2)$$

where

$$E(\varepsilon_{it} = 0) \qquad \text{var}(\varepsilon_{it}) = \sigma_{\varepsilon_i}^2$$

where R_{it} is the period-t returns on security *i,* for the period prior to the event date and R_{mt} is the market portfolio. ε_{it} is the zero mean disturbance term, where α_i, β_i, and $\sigma_{\varepsilon_i}^2$ are parameters of the market model.. In practice notable stock indexes are often used for the market portfolio such as the S&P 500 Index or the CRSP Value Weighted Index.

4.1.1. General Overview

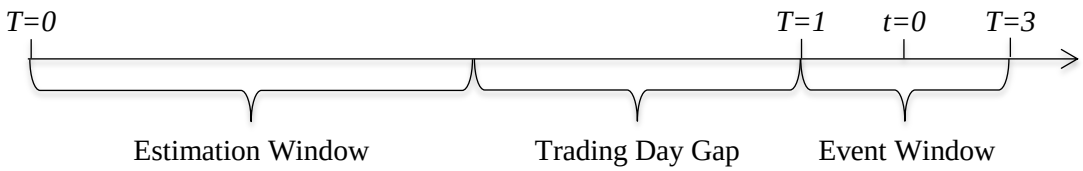
In regard to this study, the FDA drug approvals in the United States are the event of interest. The event window is the timeframe that records the abnormal return in the presence of the event. In practice it is common to expand the event window by several days prior to and after the event has taken place to capture the effects of any leaks in the days prior to the event or any fluctuations after the stock market closes on the announcement day. Since the exact approval announcement date is

occasionally uncertain (especially in the earlier time sample) a 3-day event window is applied to capture the full effect and to make it comparable across time samples, hence day -1 through day +1. If the wealth effect, or the abnormal return, in relation to the unanticipated information is significant and captured only within this event window, the market is assumed to efficient. A preannouncement window of day -10 through day -2 is applied to capture any leaks, and post-announcement window of day +2 through day +10 is applied to capture any persistence effect of the drug approval.

Given the choice of modeling the normal return, the estimation window needs to be defined. It is here the "normal returns" are estimated. The most common way to do so is to use the period prior to the event window, in this case a 250 day period prior to the event will be used. Hence, day -310 through day -60. The event window is not included in the in the estimation period to prevent the event from influencing the normal performance model parameter estimates. Further, a trading day gap between the estimation window and the beginning of the event period is established to reduce the likelihood that the risk model estimation is affected by the event-induced return variance. In this case 50 trading days are established, hence, day -60 through day -10.

Returns will be indexed in event time using t. Defining $t = 0$ as the event date, $t = T_1 + 1$ to $t = T_2$ represents the event window and $t = T_0 + 1$ to $t = T_1$ represents the estimation window, whereas $L_1 = T_1 - T_0$ to $L_2 = T_2 - T_1$ constitute the length of the estimation window and the event window, respectively. The post-event window will be from $t = T_2 + 1$ to $t = T_3$ with length of $L_3 = T_3 - T_2$. The event study is visualized in Figure 16.

Figure 16: Time Line for the Current Event Study



4.1.2. Estimation of the Market Model

Due to limitations, this paper will use only the market model. As indicated by Peterson (1989), estimations are seldom sensitive to model changes. Furthermore, Brown & Warner (1980, 1985) showed that when deriving abnormal returns from the market model, the model limits the issues

with cross-sectional correlation, and thus one can assume cross-sectional independence when applying the market model to estimate the normal returns. However, an important feature for the above statement is that Brown & Warner (1980) collected observations across many industries. In this particular case, abnormal returns are estimated from product approvals from the same industry, which increases the likelihood of cross-sectional correlation.

Additionally MacKinlay (1997) argues that market model represent a potential improvement over the constant mean return model[20], as the market model shows greater variance reduction in abnormal returns. Further, he recommends only the use of the market adjusted model when restrictions of the coefficients[21] are preferred and give better estimates.

A review of the market model is explained in Appendix 5: Market Model Framework, heavily influenced by the work of MacKinlay (1997).

4.1.3. Abnormal Performance Testing

Significance tests to assess the abnormal performance can be applied, and are often distinguished between parametric and non-parametric tests. The former rely on strict assumptions that security returns must be normally distributed, whereas the latter relaxes these assumptions (Brown & Warner, 1980).

Various significance tests are useful to account for statistical issues that the data might hold. One of the more severe issues is the event-date clustering. Events that cluster in calendar time can cause violation of cross-sectional independence that lowers the power of the cross-sectional tests or create issues from event-induced volatility when the event itself change the variance of the abnormal returns (Brown & Warner, 1980). Below, three parametric tests are briefly introduced. To verify the results from the event study analysis, all three has been applied. The definition of each test can be found in Appendix 6: Parametric Tests.

4.1.3.1. Parametric Tests

Cross-sectional t-test

One of the more simple significance tests it the cross-sectional test. This allows for increases in event-induced variance, but it still relies on the assumption that abnormal returns are cross-sectional

[20] The constant mean model is another statistical model that is consistent with the CAPM (MacKinlay, 1997).

[21] The market adjusted model restricts α to be zero and β to be one (MacKinlay, 1997).

independent (Brown & Warner, 1980). However, in a later study Brown & Warner (1985) showed that the cross-sectional test still demonstrated vulnerability to event-induced volatility. Hence, the test shows low power.

Patell's test (heteroscedastic robust)

One of the more widely used parametric tests is the Patell's test that standardized the abnormal returns from the event window. By doing so the test is robust to heteroscedastic event-window abnormal returns by assigning lower weights to abnormal returns with large variances (Patell, 1976). The test however makes implicit assumptions of cross-sectional independence and no event-induced changes in the variance of the abnormal returns around the event day.

The Patell's test is still affected by clustering volatility (Kolari & Pynnönen, 2010) and it is only appropriate to use when event-induced variance are stable (Boehmer, Masumeci, & Poulsen, 1991).

Standardized Cross-Sectional Test (variance induced robust).

To account for the situation where the variance is induced by the event itself Boehmer et al. (1991) constructed a standardized cross-sectional method replacing the abnormal returns in the cross-sectional method with standardized abnormal returns.

The implicit assumption from the above tests is that the abnormal returns are cross-sectional uncorrelated and it is often taken as a basic assumption (Brown & Warner, 1985). However, this might become an issue when event days are "common" or when firms act within the same industry. Kolari & Pynnönen (2010) showed that even with relatively low cross-correlation among abnormal return then standardized *t*-statistics from Boehmer et al. (1991) and Patell (1976) over-reject the null hypothesis of zero average abnormal returns. Hence, it is important to verify the results of the event study with several abnormal performance tests.

4.2. Ordinary Least Squares Estimation

If the outcome of the event study analysis shows a systematic change in the economic incentives to innovate, the analysis provides reasons to carry on the hypotheses testing set up in the Theoretical Framework section. To investigate what implications competition might have on the economic incentives for the firm to innovate, the Ordinary Least Squares (OLS) estimation is applied.

For many years this approach has been the work horse in empirical economics, as it allows researchers to investigate many factors that simultaneously affect the dependent variable of interest. By controlling for many factors, one can build efficient models that to a greater extent explain the variation in the dependent variable. Furthermore, researchers have the ability to apply non-linear functionality to the model by including e.g. quadratic effects or natural logarithm of the variables (Wooldridge, 2009).

A simple linear population model can be specified as:

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_K x_K + u \qquad \text{MLR } 1^{22}$$

where $y, x_1, x_2, \dots, x_K$ are random observations, u is the unobserved random disturbance term or error, and $\beta_0, \beta_1, \beta_2, \dots, \beta_K$ are parameters. The optimal purpose for the abovementioned model is to show a causal relationship between the parameters of interest and the dependent variable. A model of such kind is defined as a structural model (Wooldridge, 2011).

To ensure that OLS estimators are unbiased for the population parameters, certain assumptions[23] have to be met. The most crucial of these is the zero conditional mean assumption.

$$\mathrm{E}(u|x_1, x_2, \dots, x_k) = 0, \qquad \text{MLR 4}$$

which implies that the error term, u, has zero mean and is uncorrelated with the explanatory variables. Failing this crucial assumption causes the OLS to be biased and inconsistent. In these cases the explanatory variables x_j are said to be endogenous (as opposed to exogenous when x_j is uncorrelated with u).

Endogeneity usually arises when omitting a variable that belongs in the in the true population model. Often data for this variable might not be available, but excluding it causes the estimators to be biased.

[22] MLR is short for Multiple Linear Regression and they applied when assumption equation are explained.

[23] Appendix 7: OLS Assumptions lists all assumptions for the OLS estimators to consistent and efficient

Simultaneity also causes the zero conditional mean assumption to fail. Simultaneity arises when an explanatory variable is determined simultaneously with the dependent variable. Here the explanatory variable is partly determined by as function of y, and consequently causes the explanatory variable to correlated with the error term.

If the assumptions MLR.1 through MLR.4 in Appendix 7: OLS Assumptions hold then the OLS estimator $\widehat{\beta_J}$ is both unbiased and a consistent estimator for β_j for all $j = 0,1, \dots, k$. Further, by adding the homoscedasticity assumption MRL. 5, the OLS estimator is said to be the best linear unbiased estimator (BLUE) for the population estimator. This is also known as the Gauss-Markov Theorem.

To ensure efficient interference based on *t* and *F* statistics, the normality assumption MLR. 6 has to hold as well. By assuming the population error u is normally distributed the underlying sampling distribution of OLS estimator is also assumed to be normally distributed and the OLS has the smallest variance among unbiased estimators. The normality assumption is however very strict, requiring both MRL. 4 and MRL 5 to hold. With large enough sample sizes, one can alternatively rely on the central limit theorem and conclude that OLS estimators satisfy asymptotic normality. Thus, interference with *t* and *F* statistics can be applied if the sample distribution of $\widehat{\beta_J}$ is approximately normally distributed.

Failing on one of the consistency assumption has a more severe consequence as one cannot rely on any of the estimators obtained from the OLS. Failure of the homoscedasticity assumption MLR. 5 on the other hand has less serious consequence, as consistency of the OLS is unaffected by failure of this assumption. However, the estimators of the variances $\mathrm{Var}(\widehat{\beta_J})$ are biased without the homoscedasticity assumption and subsequent *t* and *F* statistics are invalid. It is relatively easy to get around this issue by introducing a heteroscedasticity-robust method that ensures a valid inference based on *t* and *F* statistics even if the variances of errors are not constant. In short, this method produces heteroscedasticity-robust standard errors for $\widehat{\beta_J}$ and the general inference is now valid.

4.2.1. Quadratic Effects OLS Models

The models in the regression analysis rely heavily on the quadratic effects of the main explanatory variable. However, quadratic regressions still rely on the basic OLS assumptions as the these models are linear functions of the unknown coefficients of the population regression model.

Thus, the same OLS estimations and tests can be applied on regressions included quadratic variables (Stock & Watson, 2012).

5. Event Study Analysis

The following section carries out the actual event study. The purpose of this analysis is to show whether there is evidence of any systematic changes in the firms' economic incentives to innovate.

If this might be the case, the event study analysis provides the necessary data to investigate whether the competitive implications have influenced the economic incentives for firms to innovate as predicted in the Theoretical Framework.

5.1. Data Collection

The original sample was constructed by adding pharmaceutical and biotechnology companies compiled by the Global and North American Compustat databases. Two further screens were made in order to compile the finale sample. First, to ensure that sufficient information about stock market data is available to compute the normal returns, each firm had to be included in the Center for Research in Security Prices (CRSP) database. More specifically, 300 days of stock market data prior to each drug approval had to be available to calculate the normal returns with a 250 day estimation window plus a 50 trading day gap period between estimation and event window.

Second, all firms were then cross-referenced with the FDA Drug Approval database, which had been compiled from the U.S. FDA's website. To capture the changes in the expected firm performances, drug approvals were compiled from January 1985 to November 2015[24], separated into to three 10-year cohorts: 1985-1995, 1996-2005 and 2006-2015. The FDA provides a complete database of all drug approvals in the U.S. since 1939 with the majority of patient information, labels, approval letters, and reviews available for each drug approved since 1998. All drug approval dates were obtained directly from this database. The standard procedure for the agency is to inform applicant firms on the day of the approval, and subsequently post this information on their website the same day. This allows researchers to pinpoint the exact date of a drug approval. To catch the full effect of new drug approvals, only NDAs containing NMEs[25] are included in the sample. Other chemical forms are not expected to have significant influence on the expected firm performance. In addition all BLAs were included.

[24] December 2015 was excluded to ensure enough available stock market data following the event day.

[25] See Appendix 2: FDA Regulation and an Overview of the R&D Process for chemical classifications.

The smaller sample of companies was then cross-referenced with the Factiva database to identify when the drug approvals were made public. It is worth noting that the information process in the 1980s and to a lesser extent in the 1990s was highly inefficient. The FDA Drug Approval database provides the precise date of approvals, but drug approvals were in some cases not made public made public for another 30 days[26]. After year 2000, drug approvals were published almost immediately by both the FDA itself and through voluntary company announcements. In the more recent samples, announcements were made public often late at night after market close for which the expected shareholder wealth effect is not seen until the following trading day. To account for these event date uncertainties, the expected firm performance of drug approvals, as measured in the abnormal returns, is then expected to be detected at day -1 through day +1, depending on the time of the announcement. Hence, the 3-day event window is the main focus of this study and will be used when testing the main hypotheses regarding competition and its impact on the abnormal returns.

As pointed out by MacKinlay (1997) and Peterson (1989) it is crucial to avoid any potential biases that could have been introduced through the selection process. These initial steps have been taken to avoid any bias or any confounding events around the event dates of interest:

- Deleting observations as a result of multiple classes of shares for a given company, i.e. class A and B shares.
- Manually ensure that observations falling on a non-trading day are replaced with the closest trading day.
- Excluding observations with SEC filing and/or earnings announcements in the event window (day -1 through day +1).
- Manually verifying that there is no major price relevant information in the event window (day -1 through day +1) using the Factiva database[27].
- Manually ensure that no companies overlap in the samples.
- If two or more companies co-marketed or co-developed a given drug, and both companies fit the selection criteria, the original sponsor firm is chosen as proxy to avoid a "double effect" on only one drug approval.

[26] Schering-Plough's Elocon and Pfizer's Norvasc were publicly announced 31 and 41 days after the drug was approved, respectively.

[27] This includes M&A activities, dividend payout and drugs being approved by the same company simultaneously etc.

- If joint ventures were made between two or more companies, and the joint venture is not listed, the company with the highest stake in the joint venture will be used as an approximation[28].

5.2. Data Overview

A total of 447 drug approvals met the aforementioned requirements, including 371 NMEs and 76 BLAs. Table 3 shows the approvals divided by technology, and Table 4 shows the review classifications for drugs approved.

Table 3: Drug approvals by technology

	1985-1995	1996-2005	2006-2015	Total
NME	99	140	132	371
BLA	4	32	40	76
Total	103	172	172	447
ANDA[30]	92	1,478	1,295	2,865

Table 4: Distribution of drug review classifications

	1985-1995	1996-2005	2006-2015	Total
Standard	58	111	113	282
Priority	45	61	59	165
Orphan[29]	13	27	33	73
Total	116	199	205	520

The distribution of therapeutic areas has also changed significantly through time. Table 5 shows the distribution of the top therapy areas.

[28] ViiV Healthcare (comprising GlaxoSmithKline, Pfizer and Shionogi) and TAP Pharmaceutical Products (formed by Abbott Laboraties and Takeda Pharmaceutical) are examples of such joint ventures.

[29] Note that Orphan drug status is in combination of either a standard or priority review process; hence the total number in the table exceeds the total number of approvals. The sum of standard and priority review drug approvals is 447.

[30] ANDAs are shown for comparable purposes. These generics are not included in the event study or in the OLS regression analysis. A brief explanation of ANDAs can be found in Appendix 2: FDA Regulation and an Overview of the R&D Process.

Table 5: Distribution by Therapeutic Area

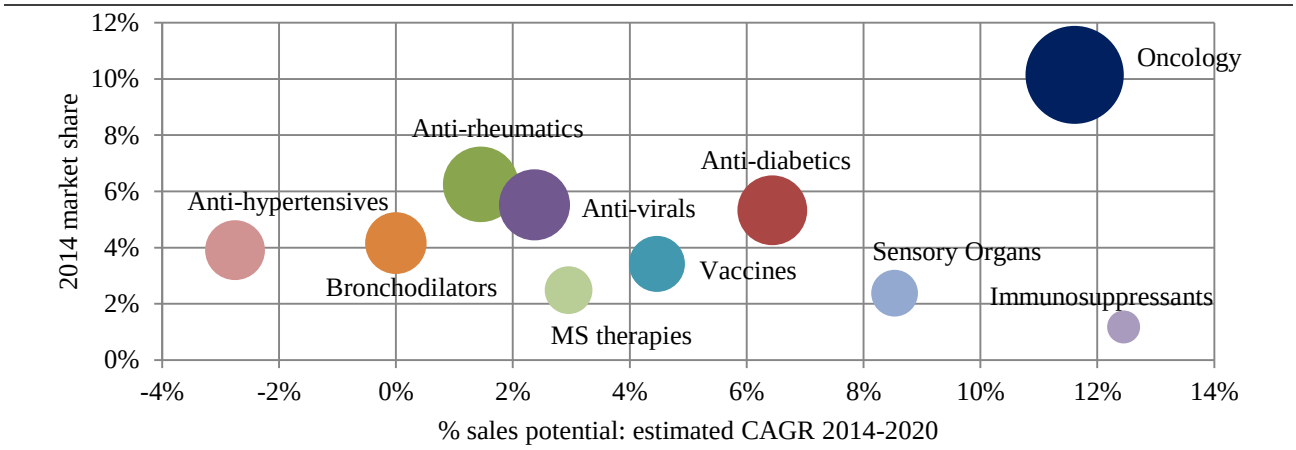
Therapeutic area	1985-1995	1996-2005	2006-2015	Total
Oncology	11	24	45	80
Metabolism	3	13	15	31
Anti-rheumatics	6	10	7	23
Anti-virals	8	19	15	42
Cardiovascular[31]	17	27	19	63
CNS	10	14	10	34
Anti-bacterials	15	23	19	57
Other[32]	32	42	44	118

Table 5 is well in line with the pharmaceuticals' pipeline focus. When analyzing market value and market potential for each therapeutic area, there is a clear link between pipeline focus and the market value/potential for the various areas. As shown in Figure 17 by 2014 oncology was by far the biggest therapeutic area with an estimated market size of USD80bn in sales. Furthermore, it is expected to have a 6-year compounded annual growth rate of 11.6% (EvaluatePharma, 2015). This is reflected in Table 5 as the number of cancer drugs approved has been rapidly increasing since the 1980s. This is also the case for anti-diabetics drugs (metabolism). In 2020, the anti-diabetic market is expected to be the second biggest market after oncology with estimated worldwide sales of USD60bn. Large markets like anti-rheumatics and anti-virals have been relatively steady for the past two decades, where cardiovascular and cardiovascular-related diseases, as well as anti-bacterials have seen a decrease in both market growth and in drug approvals.

[31] Also included under the cardiovascular area are cardiovascular-related diseases like Bronchodilators, vascular headache suppressants and Anti-hypertensives.

[32] Other therapeutic areas include painkillers, hormones, MS therapies, erectile dysfunction agents and other smaller classes.

Figure 17: Top 10 Therapy Areas in 2014, Market Share and 2014-2020e Sales CAGR

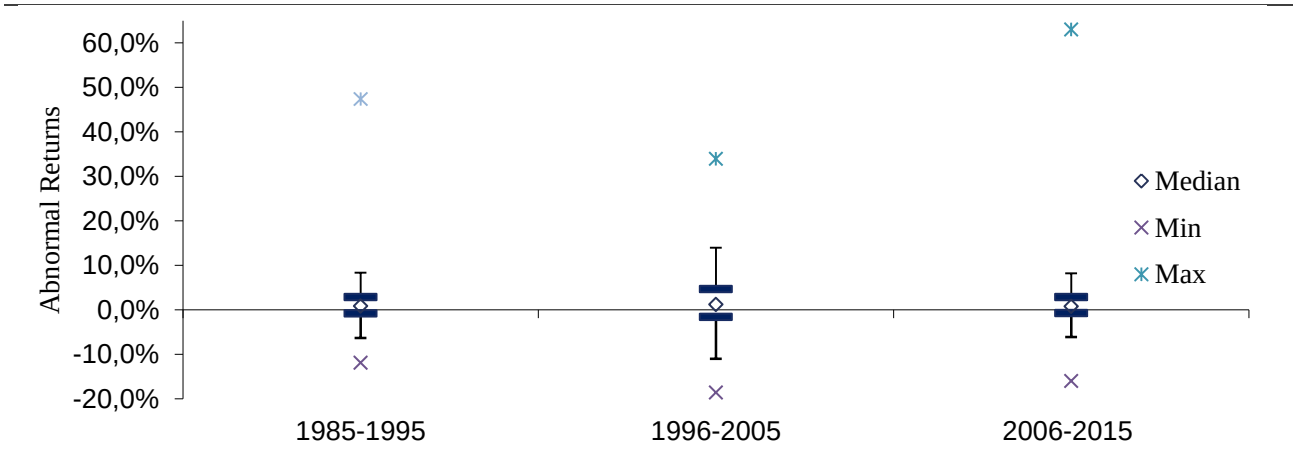


Source: (EvaluatePharma, 2015)

5.3. Outliers

There was a general suspicion of potential outliers present in the samples. Inspired by (Chambers, Cleveland, Kleiner, & Tukey, 1983), the box plot in Figure 18 shows the first quartile, the median and third quartile, as well as the maximum and minimum observation of each of the 3-day window cumulated abnormal return[33]. The fences are calculated as the interquartile times 1.5 ± lower/upper quartile. Observations beyond these fences are generally viewed as potential outliers.

Figure 18: Box Plot for Outliers



[33] The maximum observation in the 2006-2015 box plot sample is actual the second highest after the Vanda Pharmaceutical observation. The maximum outlier is excluded for visual purposes.

The following example shares some light on the issue with large outliers[34]. An observation in the 2006-2015 cohort yielded a total share price return of +900% or +600% in abnormal return on the day of the approval. In this particular case Vanda Pharmaceuticals, a small pharmaceutical company, had its first ever drug approved. Other, less extreme cases were also detected. A common dominator for all these extreme cases is firm size. For all extreme observations the belonging sponsoring firms are relatively small capitalization companies. In the Vanda Pharmaceuticals incident, at the year before its first drug approval, it had a market value of merely USD13m with no reported revenue compared to e.g. Pfizer's market value of USD119bn and USD48bn of reported revenue the same year. Interesting as it is, the valuation effect of these extreme cases might skew the focus of this paper. First indicated by Atiase (1985), smaller firms are subject to a "size effect", meaning that information production is an increasing function of firm capitalization. Hence, information availability in relation to small company drug approvals is relatively scarce for general public. In that notion, these extreme observations might not show the true value, as information is not fully available to the financial market. Many scholars however, argue that smaller firms are riskier and subsequently earn a higher return on average. However, riskiness is in many cases being misestimated due to infrequent trading (Roll, 1981), as well as generally misestimated when looking at mean returns as a consequence of lower trading volumes (Roll, 1983). Together, the market's assessments to these extreme cases might be false in reflecting the true value of a given drug approval, and consequently jeopardizing to righteously connect firm performances to economic incentives for firms to innovate. Hence, companies with a market lower than USD20m were excluded from the event study[35]. This paper however stresses the scientifically interest in these outliers, but they excluded as they would otherwise inflate the current focus of the study[36].

5.4. Event Study Empirical Results

With the full sample constructed, the event study methodology as described above was applied to investigate if the expected firm performance to new product approvals has changed significantly for last 30 years. The event study was carried out using the market model as specified in the Estimation of the Market Model section. By doing so the average abnormal return for each day in the t - 10, t +

[34] OLS regressions are highly sensitive to large outliers. Hence, it is important to deal with this issue.

[35] Excluding small capitalization companies are common in empirical studies (e.g. (Caves et al., 1975))

[36] In the Appendix 8: Event Study with Outliers the event study has been carried out including all outliers. As shown, then the cumulative abnormal return more than triples in the 3-day window in the latest sample, however there is no significant difference between the sample means.

10 event window was calculated, and then cumulated by aggregating the daily average returns over different intervals of interest.

To conduct the event study itself the Statistical Analysis System (SAS) software developed by SAS Institute was used. By collecting the necessary data through the Wharton Research Data Services (WRDS)[37], the event study was run directly through SAS.

The results of the event study analysis for the 1985-1995, 1996-2005, and 2006-2015 cohorts are displayed in Table 6, Table 7, and Table 8, respectively. For the daily average abnormal return in the event window[38], as well as for the cumulative abnormal return in the different time intervals, three abnormal performance tests, defined in Abnormal Performance Testing section, were applied to test for significance in the abnormal returns.

[37] WRDS has access to the CRSP database, which provides the daily return data needed to calculate the expected return using the market model.

[38] Note that only the average abnormal returns for each day in the t - 5, t + 5 event window are displayed.

Table 6: Event Study Analysis (1985-1995 Cohort)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0.27%	1.88*	0.96	1.13
	t-4	0.12%	0.83	1.14	1.15
	t-3	0.09%	0.54	-0.08	-0.08
	t-2	-0.17%	-1.26	-1.60	-1.75*
	t-1	0.15%	0.87	1.05	1.14
	Event day	0.96%	3.61***	5.85***	4.22***
	t+1	-0.39%	-2.29**	-2.52**	-1.93*
	t+2	0.04%	0.22	0.39	0.38
	t+3	-0.11%	-0.72	-0.53	-0.51
	t+4	0.05%	0.36	0.35	0.32
	t+5	-0.17%	-1.25	-1.04	-1.10
Number of Events		103			

Day		Cumulative Abnormal Returns			
		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	0.09%	0.13	-0.16	-0.16
2-Day Trailing	t - 1, t	1.10%	4.64***	4.85***	4.54***
2-Day Forward	t, t + 1	0.59%	1.97**	2.42**	1.85*
3-Day Window	t - 1, t + 1	0.73%	2.64***	2.58***	2.33**

*p<.10; **p<.05; ***p<.01

For 1985-1995 cohort it is shown that there was a statistical significant shareholder wealth effect from drug approvals on the day of the event (AR: 0.96%, t-statistic: 3.61, std. z-statistics: 4.22). However, on the following trading day, the abnormal return actually turns negative (AR: -0.39%, t-statistic: -2.29, std. z-statistics: -1.93). This might indicate a market overreaction to drug approvals from the day before. Several explanations can be attributed for this lagged negative reaction. First of all information regarding clinical tests is mostly available to the public through medical journals and is therefore highly specific and technical (Sarkar & de Jong, 2006). These journals are not meant for non-medical audiences, which put a barrier for retail investors to evaluate the potential of a given drug candidate. Furthermore, information disclosure by firms prior to 2000 was inefficient. It was not before year 2000, the Security and Exchange Commission (SEC) implemented the

Regulation Fair Disclosure that prohibits public firms to release full and fair disclosure of information broadly to the public. In the past firm released nonpublic information to specific entities (Chiyachantana, Jiang, Taechapiroontong, & Wood, 2004). This combined might put retail investors at a severe disadvantage because of low medical knowledge and due to the practice of selective disclosure that put vital information about drug implications in the hands of institutional investors only.

Table 6 shows that were no market effect outside the 3-day event window, t - 1, t + 1, which indicates that the unanticipated news about product approvals is reflected efficiently in the stock prices. The 3-day window was statistical significant (CAR: 0.81%, t-statistics 3.87, std. z-statistics: 3.34).

Table 7: Event Study Analysis (1996-2005 sample)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0.13%	0.53	0.10	0.07
	t-4	0.03%	0.14	0.39	0.37
	t-3	0.09%	0.36	-0.17	-0.13
	t-2	0.06%	0.35	0.45	0.45
	t-1	-0.07%	-0.38	0.06	0.06
	Event day	1.06%	3.66***	5.40***	3.96***
	t+1	0.48%	2.07**	3.60***	3.15***
	t+2	-0.35%	-1.66*	-1.03	-0.96
	t+3	0.01%	0.08	-0.07	-0.08
	t+4	0.18%	0.82	1.33	1.23
	t+5	0.06%	0.33	0.28	0.32
Number of Events		172			

		Cumulative Abnormal Returns			
Day		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	0.41%	0.54	1.15	1.28
2-Day Trailing	t - 1, t	1.02%	3.04***	3.88***	3.37***
2-Day Forward	t, t + 1	1.56%	4.90***	6.31***	5.46***
3-Day Window	t - 1, t + 1	1.50%	4.38***	5.20***	4.76***

*p<.10; **p<.05; ***p<.01

Similarly, for the 1996-2005 cohorts there was a positive and statistical significant market effect on the day of the event (AR: 1.06%, t-statistic: 3.66, std. z-statistics: 3.96). Contrary to the earlier sample the shareholder wealth effect is positive and statistically significant on the day after the event (AR: 0.48%, t-statistic: 2.07, std. z-statistics: 3.15). No significant wealth effect was detected outside the 3-day window.

Furthermore, the 3-day window was likewise statistically significant (CAR: 1.50%, t-statistics 4.38, std. z-statistics: 4.76).

Table 8: Event Study Analysis (2006-2015 sample)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0,00%	-0.01	-0.14	-0.11
	t-4	0.17%	1.51	0.65	0.72
	t-3	0.18%	1.42	1.83	1.83
	t-2	0.17%	1.37	0.45	0.47
	t-1	0.03%	0.21	0.20	0.22
	Event day	0.34%	1.72*	3.07***	2.11**
	t+1	0.45%	2.17**	3.43***	2.54**
	t+2	-0.33%	-2.55**	-1.80*	-1.93*
	t+3	-0.10%	-0.73	-0.17	-0.18
	t+4	0.12%	0.75	0.95	0.78
	t+5	-0.14%	-1.35	-0.60	-0.64
Number of Events		172			

Day		Cumulative Abnormal Returns			
		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	1.18%	2.07**	3.09***	3.29***
2-Day Trailing	t - 1, t	0.35%	1.59	2.32**	2.04**
2-Day Forward	t, t + 1	0.79%	3.83***	4.62***	3.41***
3-Day Window	t - 1, t + 1	0.81%	3.87***	3.88***	3.34***

*p<.10; **p<.05; ***p<.01

Lastly, the 2006-2015 sample showed positive and statistically significant shareholder wealth effect on the day of the event (AR: 0.34%, t-statistic: 1.72, std. z-statistics: 2.11) and on the day following the event (AR: 0.45%, t-statistic: 2.17, std. z-statistics: 2.54). However, Table 8 reveals a significant negative effect at t + 2 (AR: -0.33%, t-statistic: -2.55, std. z-statistics: -1.93), showing a lack of market efficiency in the latest time period. The market seems to respond to new information about drug approvals outside the predefined 3-day event window – i.e. outside the fences of what consider a market to be efficient. These findings raise concerns not only when it comes to the validation of market efficiency in itself in a broad perspective, but also whether the study can rely on the expected firm performance as a true reflection of the market's perception in relation to new product innovations. A pre-defined condition to treat abnormal returns as an approximation for the

economic incentives for firms to innovate is that the EMH holds, at least in its semi-strong form. That is, prices should adjust efficiently to new firm-specific information at least in so far the marginal benefits of acting on information exceed marginal costs.

Despite these rather disturbing findings regarding the market efficiency in the 2006-2015 cohort, the study assumes that the EMH holds, however in a "slightly" weaker form[39]. Thus, the abnormal returns recorded in the event study serve as a valid approximation of the economic incentives for firms to innovate.

The 3-day window was positive and statistically significant (CAR: 0.81%, t-statistics 3.87, std. z-statistics: 3.34).

Figure 19 compares the cumulative abnormal return for the 3-day event window in each time period and Figure 20 shows the cumulative effect in the 11-day window for each time period.

Figure 19: Cumulative Abnormal Return for the 3-day Event Window Across Time Periods

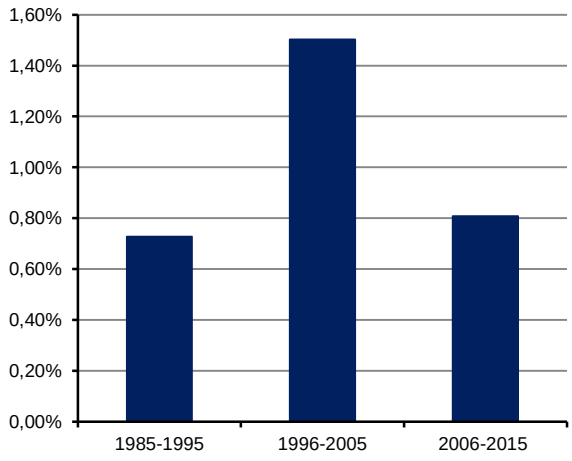
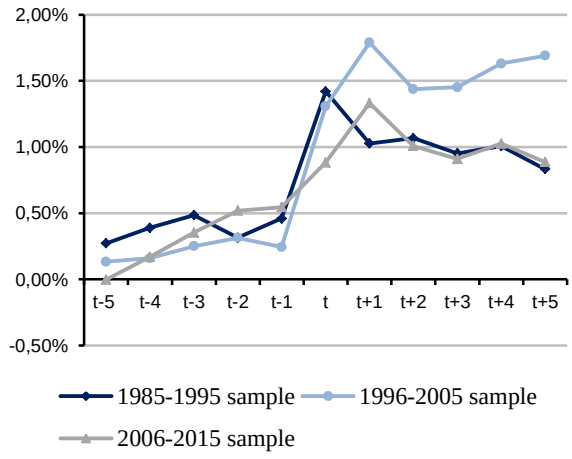


Figure 20: Cumulative Abnormal Returns for Each Time Cohort from the 11-day Event Window



Two important implications can be drawn from the above event study analyses. First and foremost, the financial markets respond *somewhat* efficiently to new information by rewarding sponsoring firms for successfully passing their drug candidate through the regulatory process with the exception of the 2006-2015 cohort, which showed evidence of a persistence effect at t+2. The study will not fail the EMH, rather it will accept in a slightly weaker form than the one specified in the Theoretical Framework, and the study will carry out the research under the assumption that the

[39] Two out three abnormal performance tests reject the null hypothesis of no abnormal returns recorded at day t +2 with a significance level of "only" 10%.

collected data represents the true market perception of the expected firm performances as a respond to new drug approvals. Hence, because of the significance of these abnormal returns, they righteously serve as an approximation for the economic incentives for firms to innovate. The study however, raises concerns for the market efficiencies in the last period and devotes these concerns to further research studies.

Secondly, there seems to be a systematic change in the expected firm performances across the time periods as measured in the magnitude of the 3-day abnormal returns[40]. The average abnormal returns from the first time period to the second jumps by 0.78%-points (from 0.73% to 1.50%) only then to drop to 0.81% in the latest time sample. If suggesting that the abnormal return reflects the true value of a given product approval on the firm value itself, the market assign higher values to product approvals obtained in the 1996-2005 time sample compared to approvals prior to and approvals following this time period; at least judge from Figure 19.

A simple *t*-test rejected the null hypothesis that the average expected firm performance between the 1985-1995 and 1996-2005 time samples were the same (*t*-stat: 1.752, $p < 0.078$). The equivalent *t*-test also rejected the null hypothesis for the average firm performance between the 1996-2005 and 2006-2015 time samples (*t*-stat: 1.729, $p < 0.085$). There was however not enough evidence to reject the null hypothesis for average firm performance difference between the 1985-1995 and 2006-2015 time samples.

In conclusion, the EMH, although in a slightly weaker form, is verified in the above event study analysis, as new information about product approval is *somewhat* efficiently impounded in the stock prices in the predefined 3-day event window. By verifying the weaker form of the EMH, the expected firm performance, as measured in the abnormal returns, serves as a validated approximation to the economic incentives for firms to innovate

Secondly, there seems to be clear evidence of a systematic change in the expected firm performance as a respond to new drug approvals for the last 30 years. The expected firm performance or firms' innovation incentives have shown an increasing trend up until the 1996-2005 cohort for then to start decreasing in the latest time cohort. Furthermore, the average abnormal returns in the 1996-2005 cohort are significantly different from average abnormal returns in the two

[40] Henceforward referred to as "abnormal return" as it is the cumulative 3-day abnormal return upcoming analyses are based on.

remaining cohorts. No evidence of a significantly difference means between the 1985-1995 and the 2005-2015 cohorts was found.

As the event study analysis showed a significant systematic change in innovation incentives for the firms it opens the door for the possibility to investigate the underlying explanation for this change. The next section will investigate the correlation between the economic incentives to innovate and competition.

6. Regression Analysis

To test *H1* and *H2* regarding competitions and its implications on the expected firm performances, the abnormal returns[41] for each drug approval obtained from the above event study analysis will be carried out in OLS regression analysis as the dependent variable of interest. The regression analysis provides the possibility to investigate the partial effect of competition on the economic incentives to innovate while simultaneously control for other factors that might influence these incentives.

The section starts by introducing the data for the OLS regression as well as to define the competitive measures used to test the main hypotheses. The results of the regression analysis will be presented followed by a discussion of the main findings.

6.1. Data for OLS regression

Before presenting the data for the OLS regression it is important to define the market first. This has important implications for the calculation of competition measures as well as for a precise definition of the control variables.

The pharmaceutical market in this paper is not limited to the North American market only despite all abnormal returns being collected on the basis of FDA drug approvals in the US. As abnormal returns in this study were constrained to event study available data only firms listed on US market was included. Many of the world's biggest companies are listed in the US, but not all[42]. However, in reality close to all firms on a global scale seek to get their product approved in the US.

[41] The abnormal returns are the cumulative abnormal return in the 3-day event window.

[42] For instance, Swiss pharmaceutical giant, Hoffman-La Roche and German-based Bayer AG are not listed in the US.

The main reason for this is that US market is by far the most valuable in the world[43]. In addition it is growing at a much faster pace[44].

The US market thus serves an approximation of the global pharmaceutical market. Consequently, when investigating the impact of competition on the abnormal returns, the competition variables, to the extent possible, have to capture the competitive pressure from the world's pharmaceutical market and not only the North American market.

6.1.1. Competition Measurements

To test the correlation between the abnormal returns and competition it is important to investigate what empirical measures of competition are appropriate for the data available. Data availability is often the main issue when researchers want to test highly theoretical competition equations in empirical studies. Researchers thus rely on various approximations of market competition.

Two popular proxies to measure market competition seem to be consistent across various research papers, namely, market concentration and profit margins. The former approximation relates to a general decrease in prices when industry concentration is high. Hence, researchers implicitly assume exogenous market structure[45]. Profit margins approximations assume that firms with relatively high profit margins operate in industries with relatively low level of competition. Clever as many of these approximations are, they generally have a number of flaws. For instance, researchers often aggregate competition measures based on industry classifications. However, by doing so researchers implicit assume the same competition pressure for each firm. By now it is clearly evident that heterogeneity across firms is present. Yet, aggression on a narrower level might disregard important geographical implications (Du & Chen, 2010).

(Du & Chen, 2010) stress the importance of applying a number of alternative measures to verify competition robustness. In this study two competition measurements are applied – a measurement of market concentration and a measurement of profit margins.

[43] See Figure 34 in Appendix 9: Figures for the Regression Analysis for illustration.

[44] See Figure 35 in Appendix 9: Figures for the Regression Analysis for illustration.

[45] When market structure is assumed to be endogenous, the relation between competition and concentration is ambiguous (Du and Chen, 2010).

6.1.1.1. Hannah and Kay index:

The Hannah Kay $\left(\mathrm{HK}(\alpha)\right)$ index relies on firms' market share. It can be written as:

$$\mathrm{HK}(\alpha) = \sum_{i=1}^{N} s_s^{\alpha}, \qquad (3)$$

where α is a parameter taken the value $\alpha > 0$ and $\alpha \neq 1$. s_i is firm i's market share and N is the total number of firms in an industry. The $\mathrm{HK}(\alpha)$ index is derived from the original Herfandahl-Hirschman index (HHI). In fact letting $\alpha = 2$ the two measures are essentially the same. An advantage to this measure stems from allowing α to take different values. If $\alpha < 2$, the index puts relatively more weight on smaller firms and less weight on larger firms, and vice versa when $\alpha > 2$. With the index approaching 1 the market is dominated by very few market participants, hence the market is defined as a monopoly market (Du & Chen, 2010).

Since the pharmaceutical industry is highly fragmented, a value of $\alpha = 1.5$ was chosen to put relatively more weights on smaller firms. Due to data limitations, subcategories within the pharmaceutical industry were identified according to the North American Industry Classification System (NAICS)[46]. Only three subcategories could be identified on the North American market – again due to data limitations. Furthermore, sales were chosen to calculate market concentration over alternatives measures like the number of employees or assets employed. For the traditional pharmaceutical industry, a firm's sales are a key value driver for growth. One could argue that for a manufacturer of biological product its value of its assets [47] is of more importance. To make the competition measure comparable across subcategories, sales are chosen for all subindustries.

6.1.1.2. Adjusted Lerner Index

A significant drawback to the $\mathrm{HK}(\alpha)$ is that it ignores heterogeneity across firms. Furthermore, it requires a strict definition of geographical and product markets. An alternative competition measure that takes into account firm heterogeneity is the measures of profit margins. It can be further measured on an industry level by aggregating competitive pressure for each individual firm. Originated from the Lerner index, Aghion et al., (2005) proposed a practical development to this measurement:

[46] See Appendix 10: NAICS Classifications for industry classifications.

[47] Most biotechnology firms only have one or few pipeline products with no reported revenue. Hence, intangible assets might be matter more for these companies as these represent the future potential for the pipeline products.

$$c_{jt} = 1 - \frac{1}{N_{jt}} \sum_{i \in j} L_{it}, \qquad (4)$$

where $L = \frac{(\text{operating profit} - \text{depreciation} - \text{provisions} - \text{estimated financial cost of capital})}{\text{sales}}$, and N_{jt} is total number of firms in industry j in year t. A value of 1 indicates perfect competition, and a value below 1 indicated some degree of monopoly.

Due to data limitation, the Lerner index by Aghion et al. (2005) was slightly changed [48]. The provision variable was dropped along with the estimated financial cost of capital. Aghion et al. (2005) themselves apply an alternative competitive measure without the financial cost since the variable is relatively small and stable over time. They find robust results for this alternative.

Contrary for this measure compared to the HK(α) is that that L is collected at a drug therapy level. By identifying the top 20 firms for each therapeutic area, L was calculated and averaged across firms within each area. Furthermore the top 20 generic companies were also added so the competition measurement reflects the competition pressure for generic competition. This gives a more sophisticated and precise measure of competition in each individual therapeutic area.

6.2. Regression Results

Before establishing a model for the regression, the variables of interest are visualized in a scatter plot. Figure 21 plots the average Lerner index on the x-axis against abnormal returns on the y-axis. Each point represents an industry average in a given year fitted with a quadratic trend line. Figure 22 plots the Lerner index against the number of total NMEs and BLAs approved.

[48] Henceforth referred to as adjusted Lerner index

Figure 21: Scatter Plot of Abnormal Returns on Competition

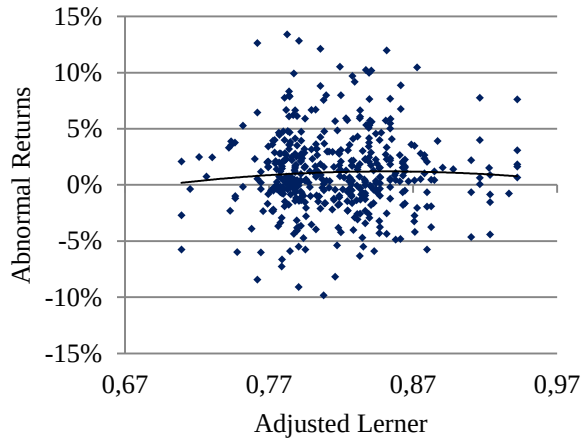
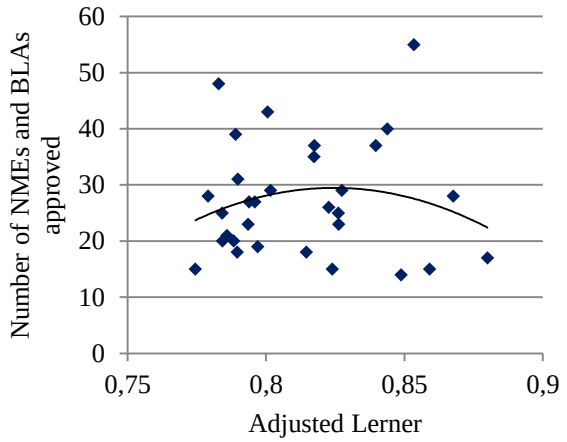


Figure 22: Scatter Plot of Number of Approved NMEs and BLAs on Competition



From the scatter plots above there seems to be a clear indication of an inverted U-shaped relationship between the economic incentives to innovate and some measure of competition.

Note that the inverted U-shaped relationship between the abnormal return and the Adjusted Lerner is less clear than when the adjusted Lerner is plotted against the number of drug approvals. If the abnormal returns represent the financial market's valuation of each drug approval, why then are the two plots not more identical? This might relate to the importance of controlling for various effects on abnormal returns that have no causal relationship with market competition. Some institutional features of the industry or the individual companies might have a spurious effect.

To test *H1* and *H2* a model is specified as followed:

$$ar_{it} = \alpha + \beta_1 Comp_{jt} + \beta_2 Comp_{jt}^2 + u_{it} \qquad (5)$$

where ar_{it}includes the abnormal returns for drug i at time t. $Comp_{jt}$ is the competition variable including a model with the adjusted Lerner index and a model with the HK(α) as specified in the Competition Measurements section. The competition measures are captured in industry j [49]at time t.

[49] As mentioned above that HK(α) is measured at an industry level according to the NAICS, whereas the adjusted Lerner index is estimated on a drug therapeutic level for each company and then aggregated. For future reference,

The squared version of $Comp_{jt}$ is to capture the quadratic effect of competition on abnormal return. The competitive indicators are further captured in the same years as the drug approvals. These indicators should reflect the current competitive environment rather than the laggard effect.

In this paper, only the model with the adjusted Lerner variable will be carried out. The full model applying the HK(α) is carried out in Appendix 11: Regression Results with HK($\boldsymbol{\alpha}$). Although generally showing the expected directions of the indicators, only the competition coefficients on the HK(α) and HK(α)^2 are statistically significant in the 1985-1995 cohort. The joint hypothesis between the competition variables and their interactions are however highly insignificant (*F*-statistic: 0.08, *p*-value: 0.78). One explanation might be the lack of variation in the competition variable. As the competition measure is only captured in three subcategories for the entire industry not enough variation is captured in the variable. On top of that the measure possesses a static nature as it only changes on yearly basis.

The main results of Model (1) are presented in Table 9. There are general signs of heteroscedasticity in the error terms; hence throughout the models heteroscedasticity-robust standard errors are applied[50]. Despite $Comp_{jt}$ and $Comp_{jt}^2$ displaying the expected directions, none is statistically significant.

There is a general suspicion of omitted variable biases with Model (1). As argued by Aghion et al. (2005), some institutional features of the industry, other than the competition measure, or some features of each individual firm might have partial effects on the abnormal returns while simultaneously correlate with the competition measures. In addition, any macroeconomic shocks to the market also need to be accounted for. Recall that the event studies were carried out in a time span of 30 years from 1985 to 2015[51].

notion *j* captures observations at the drug therapy level, whereas notion *k*, represents industry observation indentified by the NAICS.

[50] See Appendix 12: Residual Analysis for a residual analysis. In general there is evidence for the normality assumption to be true.

[51] That might be a good explanation to why the U-shaped relationship between the abnormal returns and the adjusted Lerner index in Figure 21 is not as clear as when plotting the number of drugs approved against the same measure of competition.

Schmalensee (1989) stressed that departures from long-term equilibrium might be correlated with independent variables, and hence make the estimators biased. This is often the case in capital intense industries, as firm profitability is sensitive to cyclically changes – in this case the abnormal return is sensitive to the market's continuous flow of expansions and contractions.

To account for these features several control variables are added to Model (2) (see Table 9). To encounter the effects of disequilibrium, $capital\ intensity_{k,t-1}$[52] controls for the capital intensity for industry k at time $t-1$. Schmalensee (1989) also concluded that some measures of recent sales growth successfully control for the effects of disequilibrium. Hence, the control variable $growth_{j,t-1}$, is added, which captures the lagged year on year growth in sales for therapeutic industry j. These two variables might be ambiguous as capital intensity also serves as a barrier to entry (Caves, Khalilzadeh-Shirazi, & Porter, 1975) and sales growth rates might contain information about industry demand conditions (Martin, 1984).

Du & Chen (2010) pointed out that competition measures in markets under high pressure from potential entrants might be inaccurate if incumbent firms successfully deter new market entrants, skewing the picture of the overall competitive pressure. Hence, pressure from potential market entrants might correlate with competition measure, while simultaneously having a significant influence on the abnormal results, resulting in omitted variable bias.

Caves et al. (1975) developed an approximation for barriers to entry by looking at the cost disadvantage experienced by smaller firms. The intuition behind this notion is that the relative cost disadvantage experienced by smaller firms compared to their larger counterparts serves as a barrier to entry for smaller firms – or in this case potential entrants. To capture this effect, they introduce the cost disadvantage ratio (CDR), which they defined as the average value added per employee in firms supplying approximately the bottom 50% of the value added for a given industry divided by the equivalent measure of the top 50% of the industry value added. A ratio approaching one indicates that smaller firms (or entrants) experience scale economies on the same footing as their larger firm counterparts and barriers to entry are thus relative low. As in Caves et al. (1975) the CDRs in this study were constrained to be equal to or below 1.

[52] For most control variables, the variables are lagged. This is a general method to eliminate the correlation between the explanatory variables and the error term. Furthermore, it takes time for firms to respond to industry changes.

The variable, $CDR_{j,t}$ captures the disadvantage ratio for industry j at time t. CDR is expected to be positively correlated with abnormal returns as an increase in CDR makes it easier for firms to enter, everything else being equal. Recall that the main expectation for the study is that competition is positively correlated with the economic incentives for firms to innovate.

The advertisement-to-sales ratio, $ADS_{j,t}$, was added as an additional control variable for barrier to entry. According to Comanor & Wilson (1967) advertisement intensity serves as a barrier to entry because it creates additional costs for entrants in terms of efforts for brand switching etc. Further, advertising on firm revenues creates economies of scale, which places entrants at a strong disadvantage. Hence, advertisement intensity is expected to have a negative effect on abnormal returns. Note that the barrier to entry variables is collected at the same year as the abnormal returns. These variables should reflect the current competitive pressure from entrants as were the case for the main competitive measurements.

Lastly, time dummies were added to control for various time effects. To make it comparable to the event studies, two time dummies were added: $Cohort_{1996-2005}$ equals 1 if abnormal returns were obtained in the 1996-2005 time samples and zero otherwise. The same analogy was applied for the $cohort_{2006-2015}$ variable. The model can be specified as follows:

$$ar_{it} = \alpha + \beta_1 Comp_{jt} + \beta_2 Comp_{jt}^2 + capital\ intensity_{k,t-1} + growth_{j,t-1} + CDR_{j,t} + Cohort_{1996-2005} + Cohort_{2006-2015} + u_{it} \quad (6)$$

With the control variables in Model (2) as displayed in Table 9, the competition indicators still show insignificance. In conclusion, over the total sample spanning from 1985 to 2015 the competition indicators' effect on abnormal returns fails to reflect a significant U-shaped relationship as hypothesized in the theoretical framework.

The cost disadvantages ratio is positive as expected and statistically significant at a 10% level. Hence, smaller cost disadvantages for smaller firms have a positive effect on the abnormal returns. This indicates a less severe barrier of entry, which welcomes more competition into the pharmaceutical industry. Further, some time-dependent features in 1996-2005 sample have a positive and statistically significant effect compared to the baseline period; in this case the 1985-1995 time sample. However, the joint hypothesis of the time variables is insignificant (*F*-statistic: 0.12, *p*-value: 0.729).

Given that the competition indicators are insignificant, the main hypotheses cannot be rejected, at least for the whole time period. However, to test the individual time period, as specified in the event study, separately, time interactions are included in Model (3). Despite the control variables lacking statistical significance in Model (2) they are unambiguous on the basis of theory, and are thus not excluded in Model (3). Including them would not cause any bias, but it would increase the variances of the estimated coefficients of the including variables. Further, these variables might decrease $\bar{R}^2$, but as pointed out by Wooldridge (2009) it is important not to put too much weight on $\bar{R}^2$ when evaluating econometrics models. The model specifications with corresponding coefficients are as follows:

$$ar_{it} = \alpha + \beta_1 Comp_{jt} + \beta_2 Comp_{jt}^2 + capital\ intensity_{k,t-1} + growth_{j,t-1} + CDR_{j,t} + Cohort_{1996-2005} + Cohort_{2006-2015} + Comp_{jt} \times Cohort_{1996-2005} + Comp_{jt} \times Cohort_{2006-2015} + Comp_{jt}^2 \times Cohort_{1996-2005} + Comp_{jt}^2 \times Cohort_{2006-2015} + u_{it} \quad (7)$$

In Model (3) the CDR coefficient shows robustness as the coefficient is positive and statistically significance now at a 5% level. Also the time dummies show statistically significance, however now in the opposite direction. It is difficult to specify what exactly causes these time dummies to be negative other than some institutional features in the industry other than what is already been controlled for.

The $Comp_{jt}$ and $Comp_{jt}^2$ variables in Model (3) now measure the effect on abnormal return when both the two time variables, $Cohort_{1996-2005}$ and $Cohort_{2006-2015}$ are equal to zero. Hence, the $Comp_{jt}$ and $Comp_{jt}^2$ show the partial effect on abnormal returns observed in the base period sample, which in this case is the 1985-1995 time sample. The individual coefficients' *t*-statistics are insignificant, thus there seems to be no U-shaped relationship between competition and the abnormal return in the 1985-1995 cohort. One should be careful to exclude the individual coefficient based on the individual *t*-statistic when interactions are involved. In this case $Comp_{jt}$ and $Comp_{jt}^2$ are highly correlated with the interaction terms. The joint hypothesis between the competition variables and their interactions are in fact significant at a 5% level (*F*-statistic: 5.32, *p*-value: 0.022). On the basis of this, neither the competition coefficients nor the interaction variables are dropped from Model (3).

Looking at the interaction term between the competition indicator and observations obtained in the 1996-2005 cohort, $Comp_{j,t} \times Cohort_{1996-2005}$, it's coefficient is positive and statistically significance at a 5% level. Hence, the abnormal returns captured in the 1996-2005 time sample are positively affected by competition. Additionally, competition has a statistically significant diminishing effect on the abnormal return as shown by the negative coefficient of $Comp_{jt}^2 \times Cohort_{1996-2005}$. At first glance the two interactions' coefficients seem high. An increase of one unit in the adjusted Lerner increases the abnormal return by approximately 600%. Note, as indicated in the Competition Measurements section, the adjusted Lerner index takes the value between zero and one. In a more realistic scenario an increase in the adjusted Lerner of 0.05 is investigated in an example. The mean of the Lerner index in the 1996-2005 cohort is 0.83. The below example investigate the partial effect of an increase in the Lerner index from 0.78 to the mean of 0.83. Hence, the above values of the Lerner index are plotted into the following model:

$$ar_{it} = \alpha + \beta_1 Comp_{jt} + \beta_2 Comp_{jt}^2 + Cohort_{1996-2005} + Comp_{jt} \times Cohort_{1996-2005} + Comp_{jt} + Comp_{jt}^2 \times Cohort_{1996-2005} + u_{it}$$

to investigate the partial effect on the abnormal return when the adjusted Lerner index increases from 0.78 to its mean of 0.83 holding the control variables fixed. Note that $\beta_1 Comp_{jt}$ and $\beta_2 Comp_{jt}^2$ are included in the calculation. Even though their coefficients are insignificant based on their individual *t*-statistics, excluding them from the equation will be a serious error. This is a case of multicollinearity as the $\beta_1 Comp_{jt}$ and $\beta_2 Comp_{jt}^2$ are highly correlated with the interactions terms. Since, the joint hypothesis, as shown above, rejects the competition coefficients along with their interaction terms are equal to zero, the base year is included in the above examples. Excluding these variables will show the change effect on the abnormal return on top of the base period.

From the above example, an increase in the adjusted Lerner from 0.78 to 0.83 in the 1996-2005 cohort increases the abnormal return by 0.6%.

In addition, as explained in the Hypotheses section, the economic incentive to innovate is an accelerating function of competition when the competition is at low initial level. For instance, and increase in the adjusted Lerner index of 0.05 from 0.73 to 0.78, increases the abnormal return by 1.3%.

The quadratic effect of competition has an increasing diminishing effect on abnormal return as the competition measure grows larger and eventually turns negative once a certain threshold is met. In the 1996-2005 cohort, this effect occurs when $L = \frac{6.071}{2 \times 3.615} = 0.84$. For instance an increase an increase of 0.05 in the Adjusted Lerner index from the turning point at 0.84, decreases the abnormal return by 0.3%.

Furthermore, as predicted in the Hypotheses section, the economic disincentive to innovate becomes a snowball effect as competition gets more severe after the turning point. For example an increase of 0.05 from 0.89 to 0.94 decreases the abnormal return by 1.0%.

The variables, $Comp_{j,t} \times Cohort_{2006-2015}$ and $Comp_{j,t}^2 \times Cohort_{2006-2015}$, are likewise statistical significant at a 5% level and the interpretation of these interactions works analogously with the interaction presented above. The mean value of the adjusted Lerner index in this time period is 0.79. Using the same example from above, an increase of 0.05 from 0.74 to the mean value of the adjusted Lerner index, 0.79, is associated with an increase of 0.1% in the abnormal return. Note that the increase is less than in the 1996-2005 time samples. This is due to the diminishing effect is already having taken affect when $L = \frac{6.483}{2 \times 4.162} = 0.78$ for the 2006-2015 time sample.

On the basis of these results, *H1* and *H2* cannot be rejected when looking at the entire time span of 30 years. That is, the economic incentives for firms to innovate fail to show a U-shaped related correlation with competitive forces as measured by the adjusted Lerner index.

However, when isolating the individual time periods as defined in the Event Study Analysis, both the 1996-2005 and the 2006-2015 cohorts show a significant U-shape correlation pattern with competition[53]. Hence, the recent two time periods give evidence to reject *H1* and *H2* as specified in the Hypotheses section.

The results from Model (3) are robust when adding additional industry, firm, and drug characteristics control variables in Model (4).

$R\&D\ intensity_{k,t-1}$ captures the lagged R&D investment intensity of industry k and $labour\ quality_{k,t-1}$ indicates the lagged quality of labor for industry k at time t. Both variables relates to the firms' likelihood to successfully innovate but they statistically insignificant.

[53] The results are also verified when running an OLS regression on each individual time sample.

$market\ capatilzation_{l,t}$ represents firm l's lagged market capitalization in its logarithmic form. Prior to the regression, the variable was expected to have a negative effect abnormal return. As indicated in the Outliers section the smaller firms are subject to a "size effect" first reported by Atiase (1985). Several studies have found that market reactions associated with smaller firms is larger than the market reactions to larger firm counterparts (Freeman, 1987; Womack, 1996). A "firm size-related differential information hypothesis" or "size effect" provided by Atiase (1985), stated that "the amount of private pre-disclosure information production and dissemination is an increasing function of firm size" (Atiase, 1985, p. 22). Hence, the amount of unexpected information brought to the market is inversely related to firm size. Atiase (1985) supported his hypothesis using earnings reports. He found that the degree of unexpected security price changes in response to actual earnings reports is inversely related to the market capitalization of firms.

In relation to the current study, then a sharper market reaction to drug approvals attributed to smaller firms is expected relative to their larger counterparts as these approvals are associated with more unexpected information that is not reflected in to the market. The variable verifies this as market size has negative and significant effect on abnormal returns.

Lastly, two drug-specific dummy variables were added. $Joint\ venture_{i,t}$ and $drug\ prioty_{i,t}$ take a value of 1 if a drug is approved through a collaboration, or a drug receives priority review status[54], respectively and take the value zero otherwise.

The intuition behind the $Joint\ venture_{i,t}$ variables is that riskier development projects outsourced to startups in the biotechnology industry might be a solution to avoid negative valuation effects from failures. Furthermore, McConnel & Nantell (1985) showed significant wealth gains from joint ventures, explained by the synergy hypothesis of corporate combinations. Thus, joint ventures are expected to have a positive effect on abnormal returns. Surprisingly, the coefficient in Model (4) is negative and statistically significant. A reasonable explanation for this outcome could be the size effect inflating the coefficient. It is learned that in most cases whenever two or more companies develop a drug through a collaboration of some sort, only one company applies for marketing approval at the FDA. Usually the applying company is the one that has the resources and the capacity to market drug – hence the bigger firm. Thus, whenever a drug is reported to have been

[54] See Appendix 2: FDA Regulation and an Overview of the R&D Process for drug review classifications.

approved through a joint venture, the market effect of that particular drug is measured on the firm that originally applied for the marketing approval – i.e. usually the bigger firm in that particular joint venture. Hence, the coefficient shows a negative relationship with abnormal returns as it reflects an approval for a relatively large firm. This is further verified through the positive correlation between joint venture and the firm size at 0.18.

In the case for priority drugs, they are often viewed to possess best-in-class potential, as they are granted by the FDA on the belief to represent superiority over existing therapies. Furthermore, a priority review status requires the FDA to take action following an application within six months compared to ten months under standard reviews (U.S. Food and Drug Administration, n.d.-b). Hence, drugs receiving priority review status obtain a significant advantage in the patent race.

Thus, it is expected that drugs receiving priority review classification perform better, as measured in the abnormal returns, than standard review drugs. $drug\ prioty_{i,t}$ is positive and statistically significant at a 10% level.

Table 9: Regression Analysis Models of Abnormal Returns

Dependent variable: Abnormal returns; 447 observations				
	Models			
Regressors	Model (1)	Model (2)	Model (3)	Model (4)
$Comp_{jt}$	0.861 (1.013)	0.683 (1.082)	-1.104 (1.931)	0.646 (2.106)
$Comp_{jt}^2$	-0.506 (0.610)	-0.409 (0.652)	0.676 (1.158)	-0.354 (1.258)
$capital\ intensity_{k,t-1}$		-0.001 (0.005)	-0.001 (0.005)	-0.002 (0.005)
$growth_{j,t-1}$		0.001 (0.002)	0.000 (0.002)	0.001 (0.002)
$CDR_{j,t}$		0.013* (0.007)	0.016** (0.007)	0.018** (0.007)
$ADS_{j,t}$		-0.088 (0.125)	-0.155 (0.129)	-0.078 (0.145)
$Cohort_{1996-2005}$		0.007* (0.004)	-2.536* (3.402)	-2.471* (1.396)
$Cohort_{2006-2015}$		-0.004 (0.006)	-2.529* (2.02)	-2.144 (1.328)
$Comp_{jt} \times Cohort_{1996-2005}$			6.071* (3.402)	5.886* (3.312)
$Comp_{jt} \times Cohort_{2006-2015}$			6.483** (3.258)	5.591* (3.285)
$Comp_{jt}^2 \times Cohort_{1996-2005}$			-3.615* (2.02)	-3.482* (1.964)
$Comp_{jt}^2 \times Cohort_{2006-2015}$			-4.162** (2.02)	-3.639* (2.033)
$R\&D\ intensity_{k,t-1}$				0.071 (0.046)
$labour\ quality_{k,t-1}$				-0.008 -0.005
$market\ capatilzation_{l,t}$				-0.005** (0.002)
$Joint\ venture_{i,t}$				-0.012** (0.005)
$drug\ prioty_{i,t}$				0.007* (0.003)
$Intercept$	-0.354 0.42	-0.274 0.448	0.463 0.804	-0.264 0.879
F-Statistics and *p*-Values on Joint Hypotheses				
(a) Time Variables		0.12 (0.729)	3.65* (0.057)	3.02* (0.083)
(b) $Comp$ indicators + all interactions			5.32** (0.022)	6.21*** (0.013)
(c) Global *F*-Statistic				2.18*** (0.004)
Adjusted $\bar{R}^2$	-0.002	0.002	0.011	0.043

*p<.10; **p<.05; ***p<.01

The above analysis revealed some mixed results in relation to the main hypotheses. First and foremost, the analysis fails to provide enough evidence to clearly reject the main hypotheses analyzing the partial effect of competition on the economic incentives to innovate for the entire time period from 1985 to 2015. Despite the competitive indicators showing the expected directions, none of these are statistically significant.

However, when isolating the abnormal returns in time cohorts as proposed in the event study analysis, it is revealed that the 1985-1995 cohort is the main reason to why the analysis fails to reject *H1* and *H2*. The interaction terms, $Comp_{j,t} \times Cohort_{1996-2005}$ and $Comp_{j,t} \times Cohort_{2006-2015}$ are both positive and statistically significant. This indicates that the abnormal returns – or the economic incentives, are positively influenced by more competition in the latter two time periods.

$Comp_{j,t}^2 \times Cohort_{1996-2005}$ and $Comp_{j,t}^2 \times Cohort_{2006-2015}$ are likewise significant but negative. This suggests a diminishing effect as the level of competition increases. Once a certain threshold is met, adding more competition after this turning point will decrease the abnormal return. The optimal level of competition, i.e. when the economic incentives are at their highest, for the 1996-2005 and 2006-2015 cohorts is when the adjusted Lerner index is 0.84 and 0.78, respectively. Adding more competition after this point will have diminishing effect on the economic innovation incentives.

One is tempting to draw parallels to the event study analysis and conclude that the inverted U-shaped pattern in the abnormal returns as displayed in Figure 19 is due to competition. There is no doubt that competition played a significant role to this development as verified in the regression analysis. However, there can be many industry, firm, even product related reasons for these changes in abnormal. The main objective for event study was to show that EMH holds (in a weaker form) and the economic incentives for firms to innovate have changed over time. The regression analysis showed, at least for the 1994-2005 and 2006-2015 time cohorts, that economic incentives to innovate are positively influenced by more competition, however only up to certain level for which the relationship turn negative – i.e. to show that innovation incentives follow an inverted U-shaped relationship with competition.

7. Concluding Remarks

The results derived from the event study analysis as well as from the regression analysis shed some light on the main research question posed in Introduction section.

The event study analysis brought forth two important implications. First of all, the event study analysis revealed that shareholders reward firms' innovative efforts by increasing their firm value at the time of the approvals. These rewards are shown somewhat efficiently in the stock prices as these wealth effects are recorded in the t - 1, t + 1 event window – the pre-defined window for the EMH to hold. The 2006-2015 cohort however, showed a lack of market efficiencies, as the analysis of this cohort revealed a significant persistence effect at t + 2. The study however does not abandoned the EMH due to these findings, but rather accepted it in a slightly weaker form than the semi-strong version of the EMH defined by (E. F. Fama, 1991).

As the event study verified the EMH, though in a slightly weaker form, the expected performances related to product innovations serve as a validated approximation to the economic incentives for the firm to innovate. To understand this, recall that the expected firm performance is actually an implicit measure of how the market perceive a given product innovation. By relying on the Principle of the Conservation of Values, the significant market reaction reflected in stock prices observed in the event study analysis as an efficient reaction to product approvals *must* be the shareholders' reaction to some fundamental changes to the firms' future prospect caused by these product innovations. Recall that the Principle of the Conservation of Values state that initiatives that do not increase future cash flow do not create any value. Thus, product innovations in this context create value for the overall firm, as shareholders reward the firms' innovative efforts by increasing their firm values. This in turn gives the firms economic incentives to innovate as it creates shareholder value – i.e. the main objective for firms. The incentives to innovate are thus a circular flow to the extent firms are rewarded for their innovative efforts.

Furthermore, since product approvals increase the expected performance for the overall firm, it shows that product innovation have economic implication beyond the product itself.

Secondly, the event study analysis verified that the expected firm performance related to new product approvals – or innovation incentives, have systematically changed over time. The study showed that the expected firm performances observed in the 1996-2005 cohort was on average significantly different from the two remaining cohorts. The event study analysis however, was

restricted to show the underlying causes for these changes, but it provides enough validation to carry on with the research question posed in the introduction.

In addition to show some valuable insight into the dynamics of the economic incentives for firms to innovate, the event study provided the necessary data to test the main hypotheses – i.e. to test whether the economic innovation incentives follow an inverted-U shaped relationship with the level of competition as argued in the Theoretical Framework section.

Despite a rather sophisticated competitive measure there was not enough evidence to support a clear rejection of the established null hypotheses for the whole time period, even when controlling for various macroeconomic-related effects that might biased the competitive indicators. The regression analysis thus failed to show an inverted U-shaped relationship between the economic incentives to innovate and the level of competition.

However, when isolating the time periods as proposed in the event study analysis, the 1996-2005 and 2006-2015 cohorts showed some interesting results. The competitive indicator, the adjusted Lerner index, in both cohorts was positive and statistically significant at a 10% significance level or better. This indicates that economic incentives for firms to innovate increases with the level of competition.

An intuitively explanation for this might occur from the "escaping competition" effect as proposed by Aghion et al. (2005). As competition increases, the incremental earnings for the incumbent firms to innovate also increase, discouraging potential entrants from innovating[55]. Increasing incremental earnings from new innovation should, everything else being equal, increase future cash flows, which then should be reflected in an increase in the expected firm performance once the new innovation is introduced (only if the EMH holds).

The quadratic effect in these time cohorts was also significant but negative. This indicates a diminishing effect on the economic incentives to innovate once a certain level of competition is met.

Intuitively, at some point along the curve, the incremental earnings from innovating for the incumbent firm become negative, and additional innovation efforts after this points destroy value rather than to create value. Thus, at some point competition turns the economic incentives to innovate into an economic disincentive for firms to innovate. After this threshold all innovation

[55] Recall that the incentives to innovate stems from the difference the between pre-innovation and post-innovation rent. The "escape competition" effect lowers the pre-innovation rent by more than it decreases the post-innovation rent. Hence, incumbent firms have the incentives to innovate as long as pre-innovation is greater than zero.

stems from entrants with low initial profits further exploiting post-innovation rents. In addition, as competition increases competing products move further away from the technology frontier. Hence, increasing competition after the optimal point, the economic disincentive for firms to innovate becomes a snowball effect. This was also evident in the empirical findings.

Despite failing to reject the main hypotheses for the whole sample, 1996-2005 and 2006-2015 time cohorts provide significant evidence to reject *H1* and *H2* if testing these time cohorts separately. Hence, disregarding the observation from the 1985-1995 cohorts, the current study successfully showed that competitive forces have a positive impact on the economic incentives for firms to innovate (*H1).* However, at some point along the curve too much competition replaces the positive relationship into a negative one. The study showed that excessive competition has an economic disincentive for firms to innovate (*H2*). In combination the study showed that the economic incentives for firms to innovate and competition follow an inverted U-shaped pattern.

7.1. Discussion

The findings in this study extended the burgeoning literature on product innovation by bridging it with the ideas of financial economics. With a valid connection between economic innovation and the practical usefulness of financial economics the present study brought forward knowledgeable insight to the dynamics behind the economic incentives for firms to innovate – in particular how these incentives react to competitive environment movements.

In the following subsections the current findings are discussed in relation to further research implications as well as how these findings may have implications in practice.

7.1.1. Implications for Research

The current study showed that the economic incentives for firms to innovate are positively impacted with the level of competition, at least up to a certain point where excessive competition turns the innovation incentives into an economic disincentive for firms to innovate.

The study was however limited to event study-available data for which the pharmaceutical industry was chosen as an approximation to represent the economic innovation incentives for firms across all industries. To show consistency to these findings it is necessary to replicate the above studies in other industries as well.

This raises yet another interesting question: can the financial market efficiently evaluate the different impact each product innovation might have on a given firm in a given industry? Products

from different industries vary significantly in relation to their technology complexity, market potential and influence on market shares. The question really relates to whether market efficiencies in other industries hold. If so, researchers can successfully approximate expected firm performance in relation to a given new product introduction to represent the economic incentives for firms to innovate and carry out a similar study as the one presented here.

The research question in the present study was also limited to focus on product innovation success disregarding the impact product innovation failures might have on the firm as a whole. Product failures are in particular a crucial element in the innovation development process in the pharmaceutical industry. Recall from the Pharmaceutical Industry Analysis the average costs to develop a drug are approximately USD2.6bn. Failing the regulatory process thus have a crucial financial impact, as these costs are sunk and cannot be attributed to other pipeline products.

Sharma & Lacey (2004) showed that the expected firm performance to product successes and failures are highly asymmetric. A possible explanation to this might be that the amount of uncertainty ahead of an FDA announcement is not evenly distributed. If a product development is successful, a fair amount of uncertainty regarding future revenue expectations, customer acceptance and competitor reactions are still withstanding. Contrary to a disappointment, there is a clear certainty that at least for the time being revenue and profits would not be forthcoming. Given the virtual certainty of a loss from failure to deliver, against some degree of prevailing uncertainty if the product development is successful, one could assume that the outcome of the FDA announcement is asymmetric, and product success will likely generate a less market reaction compared to product disappointments (Sharma & Lacey, 2004).

Nonetheless product innovation failures presumably have a significant impact on the expected firm performances. It could be interesting to investigate how competition might affect these performances. Everything else being equal more competition should increase the amount of uncertainty prevailing at the innovation introduction, theoretically increasing the expected firm performances. After all uncertainty is what creates the possibility for profit (Knight, 1964; Rumelt, 2005). However, implicitly more competition should increase the amount of certain loss from product innovation failures due to loss of revenue and maybe more importantly due to the loss of market share.

7.1.2. Implication in Practice

The study identifies two implications for how the findings presented above can contribute to practical implications. From a shareholder perspective the above findings show some valuable insight to how shareholders should react to competitive pressure.

First and foremost, a presumably profitable investment strategy for the common shareholder is to buy and hold the stock in the 3-day event window of a drug approval. Particularly, investments in smaller companies seem to give some serious abnormal returns (see Appendix 8: Event Study with Outliers). Remember, however the notion of "no free lunch". A greater amount of risk is attributed to these smaller firms, sometimes even more risk than rightfully accounted for (Roll, 1981). In addition, this study only focused on product innovation success and not failures. Recall, how Sharma & Lacey (2004) found the outcomes of product success and failures to be highly asymmetric. Hence, shareholders should act with caution when engaging in investment strategies based on product innovation success.

Secondly, the findings show that increased competition will not always hurt profits. In some industries increased competition, particular in industry with low initial level of competition, actually benefits the overall expected firm performances. Shareholder in these situations should not sell shares and stay away but rather buy shares.

The second practical implication relates to political incentives. Presumably the enactment of the Hatch-Waxman Act in 1984 was the right call from the government's point of view at the time despite a particular and well-referenced study showing that the Act caused the average returns from new drugs to decrease by 12% over the initial decade after the Act was implemented (US Congress Congressional Budget Office (CBO), 1998). This is a perfect example to why it may be crucial to raise product evaluations to a higher level than to the product itself. Judging from the event study analysis the expected firm performance in relation to drug approvals showed an increasing trend from 1985 to 2005. This might not be attributed to increased competition alone, as there are many moving parts within that time period but the Act itself seems not to hurt the expected firm performances in the time after the implementation.

The findings in the regression analysis, at least for two out of three time periods, showed that competition in fact has a positive impact on the economic incentives for firms to innovate. Governments should implement policy reforms that stimulate more competition, as this enhance the

economic innovation incentives for firms –innovations that in turn bring forward new path-breaking therapy treatments for the general public.

But there is a fine line for governments to actively stimulate innovation. As proved in the regression analysis, excessive competition causes disincentives for incumbent firms to innovate. Hence, political incentives can unintentionally hurt innovation rather than to stimulate it. It is then vital for governments to know where each industry is on the competition curve.

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Appendix Overview

Appendix 1: Important Drug Milestones

Table 10: Drug Milestones 1978 to 1994

Year	Early entrants	Indication
1978	Tagamet® (cimetidine), Zantac® (ranitidine)	Ulcers
1981	Capoten® (captopril), Vasotec® (enalapril)	Hypertension
1982	Procardia® (nifedipine), Calan® (verapamil)	Hypertension
1982	Zovirax® (acyclovir), Famvir® (famciclovir)	Herpes virus
1983	Sandimmune® (cyclosporin A)	Transplantation
1985	Protropin®, Humatrope®	Human growth hormone
1986	Noroxin® (norfloxacin), Cipro® (ciprofloxacin)	Antibiotic
1986	Intron A® (interferon α-2b), Roferon A® (interferon α-2a)	Cancer
1987	Mevacor® (lovastatin), Pravachol® (pravastatin)	Cholesterol reduction
1987	Retrovir® (zidovudine), Videx® (didanosine)	AIDS
1988	Prozac® (fluoxetine), Zoloft® (sertraline)	Depression
1989	Prilosec® (omeprazole), Prevacid® (lansoprazole)	Ulcers
1990	Epogen® (epoetin-α), Procrit® (epoetin-α)	Anaemia
1990	Biaxin® (clarithromycin), Zithromax® (azithromycin)	Antibiotic
1990	Diflucan® (fluconazole)	Antifungal
1991	Zofran® (ondansetron), Kytril® (granisetron)	Antiemetic
1992	Neupogen® (filgrastim)	Cancer adjunct
1993	Taxol® (paclitaxel), Taxotere® (docetaxel)	Ovarian cancer
1993	Betaseron® (interferon β-1b), Avonex® (interferon β-1a)	Multiple sclerosis
1993	Imitrex® (sumatriptan), Zomig® (zolmitriptan)	Migraine
1994	Risperdal® (risperidone)	Schizophrenia

Source: (H. Grabowski et al., 2002)

Appendix 2: FDA Regulation and an Overview of the R&D Process

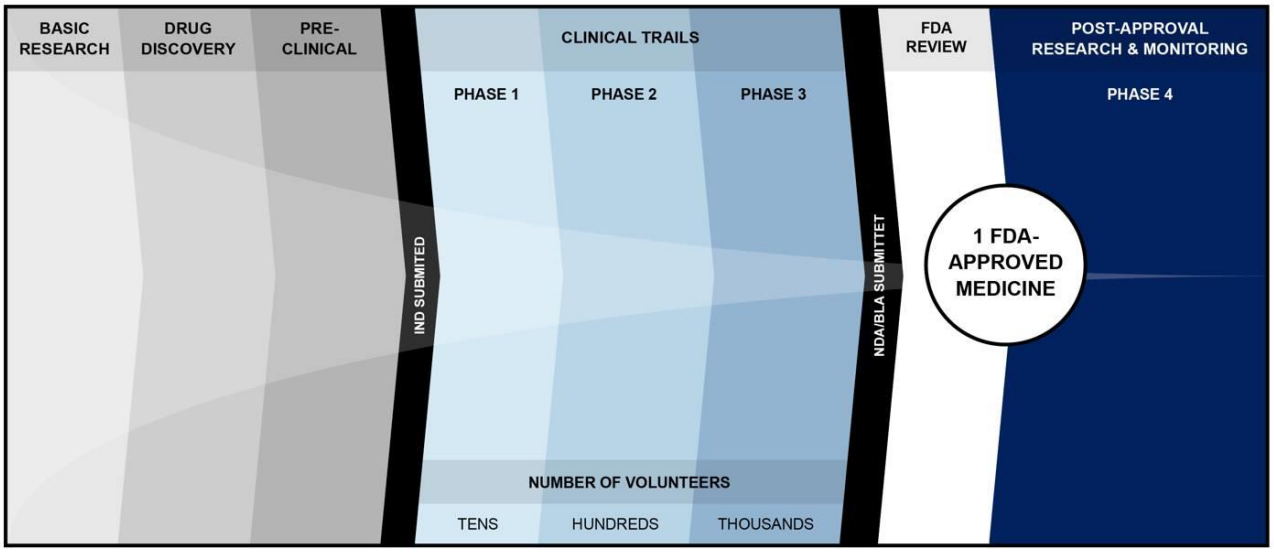
An understanding on the pharmaceutical R&D process might share some light on why it is so crucial for the pharmaceuticals to get their drugs approved, and to why delays or rejections have severe financial impact.

Governments worldwide provide regulatory oversight over the safety and quality of the products generated by medical innovation. In the United States, it is the US Food and Drug Administration (FDA) that regulates drugs, biologics, medical devices, cosmetics, radiation-emitting electronics and foods.

It was not before the enactment of the Federal Food, Drug and Cosmetic Act (FD&C Act) in 1938, the US government began screening drugs before permitting them to be sold to US consumers. Back then pharmaceuticals were only required to prove that their drugs were safe before they were allowed marketing. In conjunction with the public health scare in the 1950s where dozens of children were born with severe birth defects after their mothers treated morning sickness with thalidomide, the US Congress in 1962 amended the FD&C Act to require pharmaceuticals to show evidence of their drug's safety and efficacy.

Figure 23 displays today's drug and biologics development and approval process. With the 1962 amendment, the drug development process was broken into two parts. The first part included vitro and animal testing. Clearance from this stage leads to an Investigational New Drug (IND) application that if approved enable pharmaceuticals to initiate human clinical trials that comprise three phases. Phase I involves studies to determine the toxicology of a drug with a small number of human participants. Phase II includes medium-sized studies with hundreds participants to identify early evidence of efficacy in humans. Phase III typically include two larger well-controlled trials to prove the drug's safety and efficacy. These studies include thousands of volunteers in randomized and often double-blinded trials with the use of placebo or to greater extent direct comparable drugs (Malani & Philipson, 2012).

Figure 23: The Biopharmaceutical R&D Process



Source: (Pharmaceutical Research and Manufacturers of America (PhRMA), 2015)

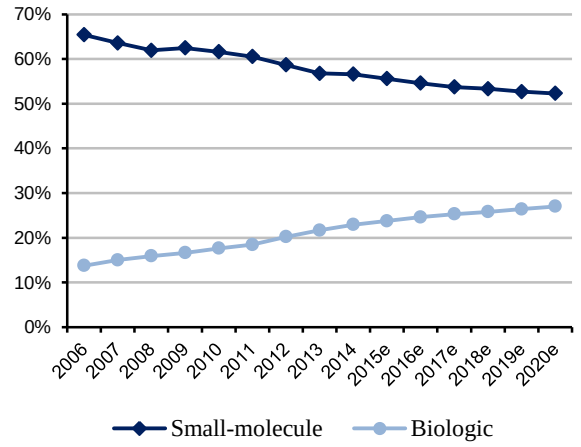
With sufficient evidence of the drug's efficacy and safety the phase III trials, pharmaceuticals may file for marketing application through two types of applications. Focusing on original drugs only (generics and biosimilars are discussed later), the FDA distinguishes between two types of drugs separated by the level of complexity of the drug structure. The less complex small-molecule drugs are approved through a New Drug Application (NDA) process. The FDA assigns NDAs on the basis of the drug's chemical type. The most noteworthy chemical types are as follows:

1. New Molecular Entity (NME): A drug containing active moiety that have not been approved for marketing.
2. New Active Ingredient: A drug that contains a new active ingredient, but with a previously approved active moiety.
3. New Dosage Form: Previously approved drug but with a new dosage form.
4. New Combination: A drug with a new drug combination of previously approved active ingredients.
5. New Formulation: A new drug, other than a new dosage form, that differs from a drug already approved (U.S. Food and Drug Administration, n.d.-a).

Biologic therapeutics, however occupy the upper end of the complexity scale. The FDA approves these high complexity medications through a so-called Biological License Applications (BLA) (Koyfman, 2013).

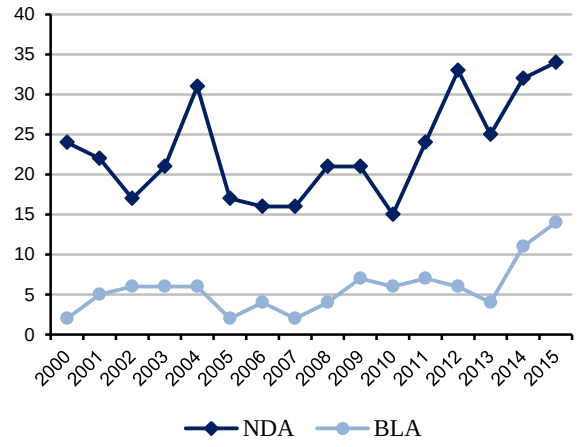
The majority of drugs approved today are small-molecule drugs (NDAs), however the number of biologics (BLAs) being approved by the FDA is ramping up (Figure 25). Further, the share of sales generated from biologics is steadily increasing (Figure 24). In 2014, 44% of the top 100 products are biotics compared to only 21% in 2006.

Figure 24: Share of Worldwide Prescription Drug Sales: Small-Molecule Vs. Biologics Technology



Source: (EvaluatePharma, 2013, 2015)

Figure 25: FDA Approvals: NDAs Vs. BLAs



Source: (U.S. Food and Drug Administration, n.d.-a)

The 1962 amendment came without issues, and concerns were raised regarding the incentives for pharmaceuticals to innovate and develop drugs for rare dieses, long FDA review times, as well as monopoly-like conditions for pharmaceutical industry in general.

The 1983 Orphan Drug Act that balanced the incentive to innovate drug treatment for rare diseases affecting fewer than 200,000 people annually with tax credits and seven years of market exclusivity to offset their clinical testing costs.

The Congress took action to address the issues concerning reduced effective patent life for new drugs and the lag of general competition in the industry by enacting the Drug Price Competition and Patent Term Restoration Act (also known as the Hatch-Waxman Act) in 1984. Prior to 1984 generic competition was close to non-existing. The key objective for the Hatch-Waxman Act was to balance the pressure from the general public and pharmacy benefit management firms (PBMs) to cost costs on medication while at the same time making sure to maintain the incentives for innovations through development of new drugs.

The Act established an Abbreviated New Drug Application (ANDA) process that reduced the cost of completing an FDA application of a generic drug significantly. Prior to the act, generic

versions had to replicate many of the same expensive clinical procedures as the original drug. With the Act generic companies only have to demonstrate that their products contain the same active ingredients as their brand-product counterparts. Further, the Act allowed generic companies to start researching the original drug prior to the patent expiration so that a generic version is ready for launch immediately after the original branded drug runs of patent. In addition, the Act, under the so-called Paragraph IV challenge, allowed generic companies to "challenge" branded product before they expired. There is even a "challenge-race" for generics to file for a Paragraph IV challenge, as it gives the "winner" a 180-day period of exclusivity before other generics can enter the market. The generic manufacturer that comes first tends to only lower the price modestly in the period of exclusivity before dropping it extensively when other generics hit the market (H. Grabowski et al., 2013; Saha, Grabowski, Birnbaum, Greenberg, & Bizan, 2006)

To balance the provisions for generic competition, the Act also promoted incentives to foster innovation for branded drug manufacturers. To a large extent that included the opportunity to receive additional patent extension through a patent term restoration that extended the life of a patent by up to 5 years. Potentially a lifetime of patent on a drug could be extended to but not exceeding 14 years. The aim was to compensate drug manufacturers for the expensive and time-consuming clinical trials on drug that is required before applying to the FDA for marketing approval (H. Grabowski et al., 2013).

The Congress addressed the issues of long FDA review times in 1992 with the Prescription Drug Users Fee Act (PDUFA). The PDUFA required companies to pay a user fee to speed up the regulatory approval process, in return for the FDA to commit to review completion deadlines (Malani & Philipson, 2012). With the PDUFA, the FDA created a two-tiered system of review times – a Standard Review and a Priority Review. A Priority Review requires the FDA to take action following an application within 6 months compared to 10 months under standard reviews. Priority Reviews are granted if the drug in question shows significant improvement in safety and effectiveness or prevention of serious conditions when compared to standard applications (U.S. Food and Drug Administration, n.d.-b).

A relatively new form of competition is posing yet another threat to the never-resting pharmaceutical industry through the Biologics Price Competition and Innovation Act (BPCIA) signed into the law in March 2010. This is an erosion threat to the market for biologics.

Where the abbreviated review for the small-molecule drugs was allowed with the 1984 Hatch-Waxman Act, the biologics equivalent, the so-called "biosimilars", was not allowed before the implementation of BPCIA in 2010. One important point of differentiation between the two acts, is that unlike generic drugs that are direct copies of branded drugs, biosimilars are considered highly similar to the approved biologic. Biosimilars can then be either approved as interchangeable, a complete substitute to the original biologic (however at a lower price), or as a biosimilar where they will be considered as an alternative treatment rather than an equivalent, yet again to a lower price (Koyfman, 2013).

With the new BPCIA the biologic market can potentially come under the same pressure as small-molecule drugs experienced with the entry of generic competition. However, it was not before March 2015 that Novartis' Zarxio, a biosimilar version of Amgen's cancer biologic Neupogen, was approved by the FDA. Additional, many uncertainties surrounding pricing strategies and whether cost-savings will be passed on to the U.S. health care system remain to be seen. But drawing parallels with the European market , where Novartis' biosimilar just four years after the European Medicines Agency (EMA) approval overtook Amgen's Neupogen as the market leader, the implementation of the BPCIA will put more pressure on pharmaceutical market going forward (Royzman, 2015), especially when biosimilars are expected to be launch with a 25-30% discount to its original biologics.

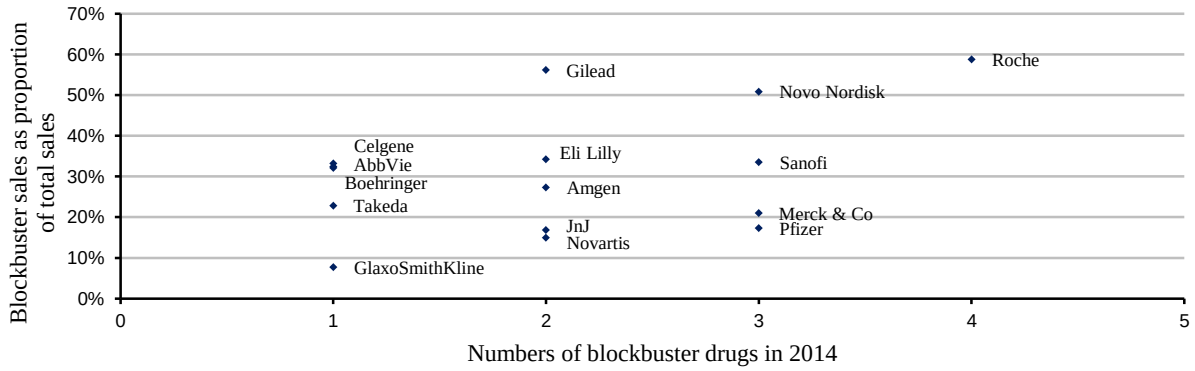
Appendix 3: Block Buster Imperative Strategy

An increasing risk for the virtuous rent seeking pharmaceuticals is the heavy reliance on only a few high–volume products to fund future pipeline products. Failing a life-cycle investment thus have a huge financial impact. The virtuous rent seeking model can further be linked to what scholars have labelled as the Blockbuster Imperative Strategy – a growth strategy pursuing development of drugs with at least USD1bn in annual sales.

For the past many decades, the pharmaceutical companies have relied heavily on the Blockbuster Imperative strategy. The economic motivation of this strategy is the relatively high returns compared with those for lower value drugs, as a substantial amount of risk is attributed to these drugs with a corresponding probability of economic gain as a reward. Additionally, these drugs offer a more sustainable growth than those achieved by patent defense strategies (Gassmann et al., 2008).

In 2014, 8 companies out of the top 20 pharmaceutical companies had one-third of their revenue earned from blockbuster products[56] (Figure 26). Sales of blockbuster drug also vary significantly, from Gilead's Sovaldi with 2014 sales of USD10.3bn to AstraZeneca's (shared with Shionogi and Chiesi) Crestor generating USD2.0bn in 2014.

Figure 26: Contribution of Blockbuster Sales to Ethical Sales in 2014



Source: (EvaluatePharma, 2015)

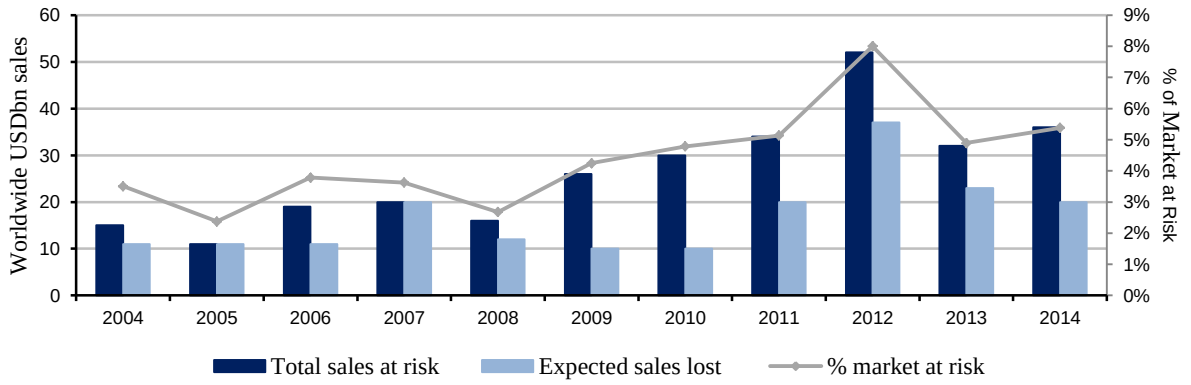
The blockbuster strategy and the virtuous rent seeking model are interchangeable. They essentially lead to the same outcome. The virtuous rent seeking pharmaceutical invest in products

[56] Using the thinking from (Gassmann et al., 2008), a blockbuster drug is defined as a drug with more than USD2bn in annual sales. Also, when more than one firm is responsible for manufacturing/marketing the annual sales from a given drug is divided evenly among firms.

that will create the most rents (blockbusters). This leads to only a few products that are responsible for funding new rent seeking products.

As a consequence of the narrowed search for compounds with blockbuster potential, many current blockbuster drugs face patent expiry with limited new drugs to replace them – also known as the patent cliff. For the past 10 years approximately USD300bn worth of revenue were or are at risk from patent expiry equivalent to 5% of the total market over the same period (Figure 27).

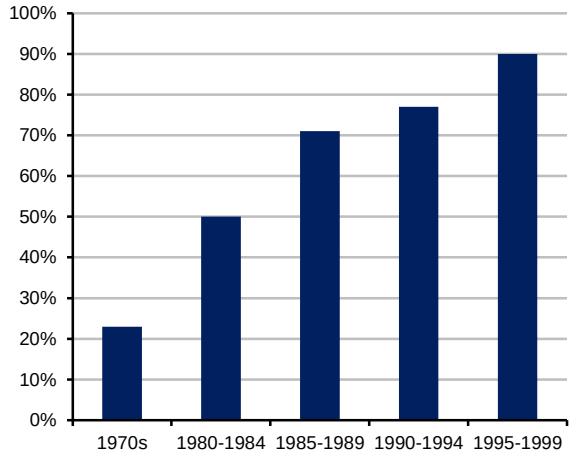
Figure 27: Total Worldwide Sales at Risk (LHS) and as % of total market (RHS) from Patent Expiry 2004-2014



Source: (EvaluatePharma, 2013, 2015)

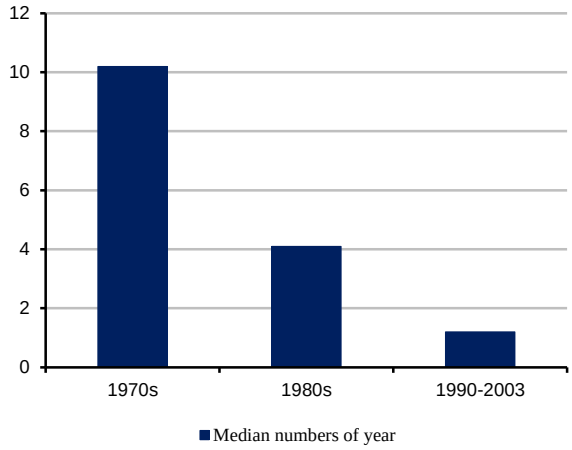
Appendix 4: Figures for the Pharmaceutical Industry Analysis

Figure 28: Percentage of First-in-Class Medicines With a Competing Product in Phase II Clinical Testing



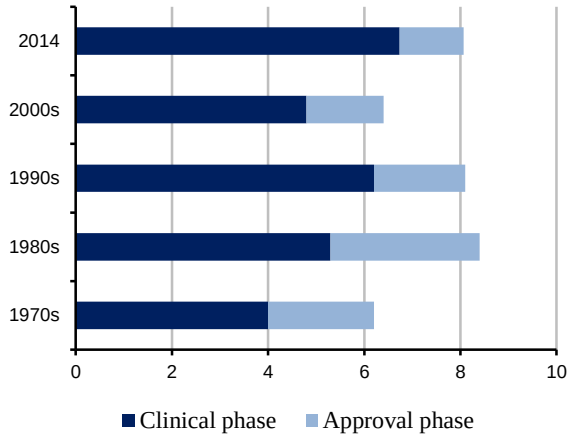
Source: (DiMasi & Faden, 2009)

Figure 29: Number of Years Between Approval of First and Second Drugs in a Therapeutic Class



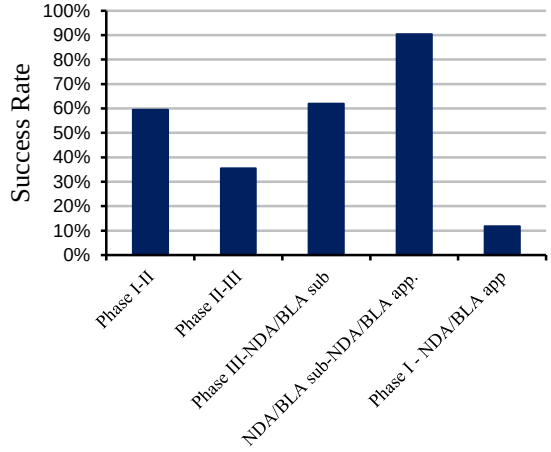
Source: (Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2009)

Figure 30: Time Spent by a Drug Candidate in the Clinical and Approval Phases (Years)



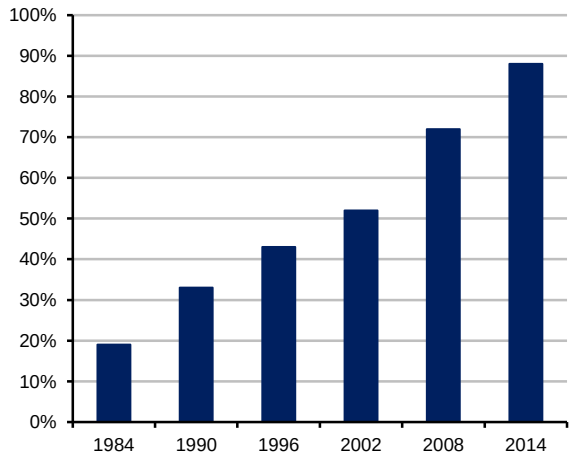
Source: (Gassmann et al., 2008; Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2014)

Figure 31: Clinical Phase Transition- and Overall Clinical Approval Success rate (1995-2007)



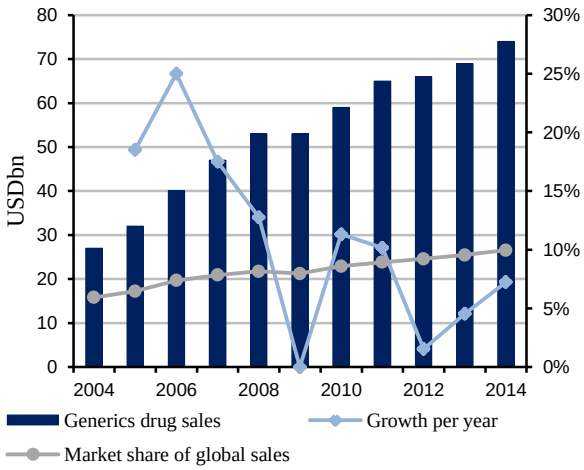
Source: (Tufts Centre for the Study of Drug Development (CSDD) Briefing, 2014)

Figure 32: Generic Share of Prescriptions Filled



Source: (Pharmaceutical Research and Manufacturers of America (PhRMA), 2015)

Figure 33: Generic Drug Sales (in USDbn), Growth and Market share (in %)



Source: (EvaluatePharma, 2013, 2015)

Appendix 5: Market Model Framework

Under general conditions, ordinary least squares (OLS) estimation is a consistent estimation procedure for the market model parameters. Additionally, given the general assumptions for statistical models from above, the OLS is efficient. For the i^{th} firm in event time, the OLS estimators of the market model parameters for an estimation window of observations are

$$\widehat{\beta_1} = \frac{\sum_{t=T_0+1}^{T_1}(R_{it}-\widehat{\mu_i})(R_{mt}-\widehat{\mu_m})}{\sum_{t=T_0+1}^{T_1}(R_{mt}-\widehat{\mu_m})^2} \quad (8)$$

$$\widehat{\alpha_i} = \widehat{\mu_i} - \widehat{\beta_i}\hat{\mu}_m \quad (9)$$

$$\hat{\sigma}_{\varepsilon_i}^2 = \frac{1}{L_1-2}\sum_{t=T_0+1}^{T_1}\left(R_{it} - \hat{\alpha}_i - \hat{\beta}_i R_{mt}\right)^2 \quad (10)$$

where

$$\hat{\mu}_i = \frac{1}{L_1}\sum_{t=T_0+1}^{T_1} R_{it}$$

and

$$\hat{\mu}_m = \frac{1}{L_1}\sum_{t=T_0+1}^{T_1} R_{mt}$$

R_{it} and R_{mt} are the return in the event period t for security i and the market, respectively. Given the market model parameter estimates above, one can measure and analyze the abnormal returns. Using the market model to measure the normal return, the sample abnormal return is

$$AR_{it} = R_{it} - \hat{\alpha}_i - \hat{\beta}_i R_{mt} \quad (11)$$

Thus, the abnormal return is the disturbance term of the market model calculated on an out of sample basis. So under the null hypothesis, conditional on the event window market returns, the abnormal returns are jointly normally distributed with a zero conditional mean and conditional variance $\sigma^2(AR_{it})$ where

$$\sigma^2(AR_{it}) = \sigma_{\varepsilon_i}^2 + \frac{1}{L_1}\left[1 + \frac{(R_{mt} - \hat{\mu}_m)^2}{\hat{\sigma}_m^2}\right] \quad (12)$$

From the above the conditional variance has two components. First, the disturbance variance $\sigma_{\varepsilon_i}^2$ from the market model, and second the additional variance due to the sampling error in α_i and β_i. This sampling error will lead to serial correlation of the abnormal returns. However, as the estimation window L_1 becomes large enough, the additional variance term approaches zero as the sampling error of the parameters vanishes. Thus, through time the variance of the abnormal return will become the first component $\sigma_{\varepsilon_i}^2$ and the abnormal return observations become independent over time. Hence, it is essential to make the estimation window large enough so that the second component to the variance is zero.

Under the null hypothesis that the event has no impact on the behavior of returns i.e. mean or variance, one can use the distributional properties of the abnormal returns to draw inferences over any period within the event window. Under H_0 the distribution of the sample abnormal return of a given observation in the event is

$$AR_{it} \sim N\big(0, \sigma^2(AR_{it})\big) \quad (13)$$

To draw overall inferences for the event of interests, the abnormal return observations must be aggregated. This aggregation will be drawn over two dimensions, i.e. through time and across securities. Starting with aggregation through time for an individual security, the concept of a cumulative abnormal return is essential to accommodate a multiple period event window. Define $CAR_i(t_1, t_2)$ as the sample cumulative abnormal return (CAR) from t_1 to t_2, where $T_1 < t_1 \leq t_2 \leq T_2$. The CAR from t_1 to t_2 is the sum of the included abnormal returns,

$$CAR_i(t_1, t_2) = \sum_{t=t_1}^{t_2} AR_{it} \quad (14)$$

And as L_1 increases the variance of CAR_i is

$$\sigma_i^2(t_1, t_2) = (t_2 - t_1 + 1)\sigma_{\varepsilon_i}^2 \qquad (15)$$

The distribution of the cumulative abnormal return under H_0 is

$$CAR_i(t_1, t_2) \sim N\left(0, \sigma_i^2(t_1, t_2)\right) \qquad (16)$$

Given the null distribution of the abnormal return and the cumulative abnormal return, test of the null hypothesis can be conducted.

It is necessary to aggregate the abnormal return observations for the event window and across observations of the event. To aggregate these observations, it is assumed there is no clustering. The absence of any overlap and the maintained distributional assumption imply that the abnormal returns and the cumulative abnormal returns are independent across securities. The abnormal return for each security, which can be calculated using $AR_{i\tau}$ for each event period. Given N events, the sample aggregated abnormal returns for period t is

$$\overline{AR_t} = \frac{1}{N}\sum_{i=1}^{N} AR_{it} \qquad (17)$$

And for large L_1, its variance is

$$\text{var}(\overline{AR_t}) = \frac{1}{N^2}\sum_{i=1}^{N} \sigma_{\varepsilon_i}^2 \qquad (18)$$

The average abnormal returns can then be aggregated over the event window. For any interval in the event window

$$\overline{CAR}(t_1, t_2) = \sum_{t=t_1}^{t_2} \overline{AR_t} \qquad (19)$$

$$\text{var}(\overline{CAR}(t_1, t_2)) = \sum_{t=t_1}^{t_2} \text{var}(\overline{AR_t}) \qquad (20)$$

One can then form the CAR's security by security and aggregate through time.

$$\overline{CAR}(t_1, t_2) = \frac{1}{N}\sum_{i=1}^{N} CAR_i(t_1, t_2) \qquad (21)$$

$$\text{var}(\overline{CAR}(t_1, t_2)) = \frac{1}{N^2}\sum_{i=1}^{N} \sigma_i^2(t_1, t_2) \quad (22)$$

(MacKinlay, 1997)**.**

The hypothesis for an event study is then to test the presence of average abnormal return H_1 against the null hypothesis of non-zero abnormal return H_0, hence:

$$H_0: \mu = 0$$
$$H_1: \mu \neq 0$$

for each of the predefined time samples.

Appendix 6: Parametric Tests

Cross-sectional t-test

The cross sectional t-test is defined as:

$$t_{CS} = \frac{\frac{1}{N}\sum_{i=1}^{N} AR_{i\tau}}{\sqrt{\frac{1}{N(N-d)}\sum_{i=1}^{N}\left[AR_i - \frac{1}{N}\sum_{i=1}^{N} AR_i\right]^2}} \qquad (23)$$

Under the null hypothesis of no abnormal performance, the cross-sectional t-test is distributed as Student-*t* with *M – 2* degrees of freedom[57]. To run the test with CAR then, the AR is simply replaced by CAR in equation 23.

Patell's test (heteroscedastic robust)

The Patell's test is defined as:

$$SAR_{i,\tau} = \frac{AR_{i\tau}}{S_{AR_{i,t}}} \qquad (24)$$

The standard error is adjusted by the forecast error to account for the out-of-sample prediction in the event window, hence:

$$S_{AR_{t,i}} = S_{AR_i}\sqrt{1 + \frac{1}{M_i} + \frac{\left(R_{m,t} - \overline{R_m}\right)^2}{\sum_{t=T_0}^{T_1}\left(R_{m,t} - \overline{R_m}\right)^2}} \qquad (25)$$

where $\overline{R_m}$ refers to the mean of the market return derived from the estimation window. Under the assumption of cross-sectional independence and constant variance over time for abnormal returns, $SAR_{i,\tau}$ is distributed as Student-*t* with *M – 2* degrees of freedom. Testing the null hypothesis of no abnormal performance is then given by:

[57] The degrees of freedom depend on the estimation of the standard deviation of abnormal returns. For the market model the standard deviation is $S_{AR_i}^2 = \frac{1}{M_i - 2}\sum_{t=T_0}^{T_1}\left(AR_{i,t}\right)^2$ with the degrees of freedom *M – 2*, where *M* denotes the number of non-missing returns in the estimation window (Serra, 2002).

$$t_{Patell} = \frac{\sum_{i=1}^{N} SAR_t}{S_{\left(\sum_{i=1}^{N} SAR_t\right)}} \qquad (26)$$

where $\sum_{j=1}^{N} SAR_t$ is the average over the sample of the standardized abnormal returns ($ASAR_t$) with zero expected value of $SAR_{i,\tau}$and the standard deviation defined as:

$$S_{(ASAR_t)} = \sqrt{\sum_{i=1}^{N} \frac{M_i - d}{M_i - 2d}} \qquad (27)$$

To run the test with CAR, then the standardized abnormal returns is cumulated over time. Hence, testing the null hypothesis of no cumulative abnormal performance is given by:

$$t_{Patell} = \frac{1}{\sqrt{N}} \sum_{i=1}^{N} \frac{\sum_{t=T_1+1}^{T_2} SAR_{i,t}}{S_{\left(\sum_{t=T_1+1}^{T_2} SAR_{i,t}\right)}} \qquad (28)$$

where $\sum_{t=T_1+1}^{T_2} SAR_{i,t}$ is cumulated standardized abnormal returns ($CSAR_t$) with zero expected value of $CSAR_{i,\tau}$and the standard deviation defined as:

$$S_{(CSAR_t)} = \sqrt{T_2 - T_1 \frac{M_i - 2}{M_i - 4}} \qquad (29)$$

Standardized Cross-Sectional Test (variance induced robust).

The standardized cross-sectional test is defined as:

$$z_{SCS} = \frac{ASAR_t}{\sqrt{N} S_{ASAR_t}} \qquad (30)$$

Where $ASAR_t$ equals to $\frac{1}{N} \sum_{j=1}^{N} SAR_{it}$, as in Patell's test and with standard deviation defined as:

$$S_{ASAR_t} = \frac{1}{(N-1)} \sum_{i=1}^{N} \left[SAR_{i,t} - \frac{1}{N} \sum_{l=1}^{N} SAR_{l,t} \right]^2 \qquad (31)$$

Note, that the standard deviation is simply standardized from the standard deviation derived from the cross-sectional test. To run the test with CAR, the AR is simply replaced by CAR in equation (31). If the event date variance is proportional to the estimation window variance and is similar across securities then it assumed to be distributed unit normal (Serra, 2002).

Appendix 7: OLS Assumptions

This section summarizes the MLR assumptions for the OLS estimator to be, unbiased, efficient and consistent estimator of the population estimator.

The first assumption simply states the true population model, and that the model is linear in the parameters. This, however, does not limit the model to be linear exclusively, as the dependent and the independent variable can arbitrary functions of the underlying variables of interest.

The second assumption states that the sample observations are drawn randomly from the population following the model in Assumption MLR.1. Hence:

$$\{(x_{i1}, x_{i2}, x_{ik}, \dots, y_i): i = 1,2, \dots, n\} \qquad \text{MLR 2}$$

Assumption MLR 3 ensures no perfect collinearity. Hence, none of the independent variables in the sample is constant and there is no perfect linear correlation between these variables. An important implication to assumption is that it still allows for correlation between the explanatory variables, but they cannot be perfectly correlated.

The last assumption for the OLS estimates to be unbiased is the zero mean condition for the error term:

$$\mathrm{E}(u|x_1, x_2, \dots, x_k) = 0 \qquad \text{MLR 4}$$

This represents the most important condition for the OLS to be unbiased. Conceptually, Assumption MLR.4 means that the error term, u, has a zero mean and is uncorrelated with the explanatory variables. Several reasons may cause Assumption MLR.4 to fail including omitted variables, measurement errors and simultaneity. As indicated, then this assumption is crucial, as failure to this condition causes all OLS estimates to be biased.

Under these four assumptions the OLS estimators are unbiased estimators for the population parameters. Further, under these assumptions the OLS estimator $\widehat{\beta_j}$ is consistent for β_j for all $j = 0,1, \dots, k$.

To ensure efficiency for the OLS estimators a homoscedasticity assumption is added:

$$\mathrm{Var}(u|x_1, \dots, x_k) = \sigma^2 \qquad \text{MLR 5}$$

This assumption ensures that the error term u has the same variance given any values of the explanatory variables. Failing this assumption, the model exhibits heteroscedasticity. Stated differently, then Assumptions MLR.5 says that the variance of y given x_k, does not depend on the values of the independent variable. By adding this assumption to the aforementioned assumptions, one can obtain the variance of the OLS estimators:

$$\mathrm{Var}(\hat{\beta}) = \frac{\sigma^2}{SST_j(1-R_j^2)}, \qquad (32)$$

for $j = 1,2, \dots, k$. Hence, if assumption MLR.1 through MLR. 5 hold, then $\mathrm{E}(\hat{\sigma}^2) = \sigma^2$. Further, by adding the fifth assumption then the OLS estimators $\widehat{\beta_J}$ are said to be the best linear unbiased estimator (BLUE) of β_j. This is known as the Gauss-Markov Theorem. And important implication to this theorem is that once obtained, then the OLS is the best estimator if the model specified is expressed as a linear function of the data on the dependent variable. Failing one of the aforementioned assumptions, the Gauss-Markov Theorem fails and might not be the best estimator for linear functions.

To draw any meaningful inference from the OLS estimates it is essential to know the full sampling distribution of the OLS estimator $\widehat{\beta_J}$. Even if the Gauss-Markov Theorem holds the distribution of $\widehat{\beta_J}$ can have any possible shape. In multiple OLS estimation the sample distribution of $\widehat{\beta_J}$ depends on the underlying distribution of the errors. Thus, to give an indication of $\widehat{\beta_J}$'s sampling distribution, it assumed that the unobserved errors are normally distributed in the population:

$$u \sim \mathrm{Normal}(0, \sigma^2), \qquad \text{(MLR 6)}$$

Hence, the population error u is independent of the explanatory variables and is normally distributed with zero mean and variance σ^2. This imposes a much stronger assumption than any previous assumptions mentioned. If one assume normality for the errors then assumptions MLR. 4 and MLR.5 cannot be violated. Assumptions MLR.1 through MLR.6 are referred to as the classical linear model (CLM) assumptions. Adding assumption MLR.6 implies that the OLS estimator has the smallest variance among unbiased estimators.

If the CLM assumptions hold then the OLS estimators are normally distributed:

$$\widehat{\beta_j} \sim \text{Normal}\left[\beta_j, \text{Var}\left(\widehat{\beta_j}\right)\right], \qquad (33)$$

When OLS estimators follow a normal distribution exact interference based on *t* and *F* statistics can be carried out. The very strict assumption in MRL.6 need not be satisfied to rely on *t* and *F* statistics. Using the central limit theorem, the OLS estimators satisfy the asymptotic normality in large enough sample sizes (Wooldridge, 2009, 2011).

Appendix 8: Event Study with Outliers

Table 11:Event Study Analysis (1985-1995 sample)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0.39%	2.46**	1.44	1.62
	t-4	0.06%	0.39	1.06	1.07
	t-3	0.08%	0.43	0.04	0.04
	t-2	0,00%	0.01	-1.15	-1.26
	t-1	0.40%	1.94*	2.00**	1.90*
	Event day	1.19%	3.05***	6.36***	4.21***
	t+1	0.01%	0.03	-1.02	-0.66
	t+2	0.12%	0.52	0.71	0.62
	t+3	-0.24%	-1.28	-0.76	-0.73
	t+4	-0.04%	-0.2	-0.1	-0.09
	t+5	-0.1%	-0.72	-0.86	-0.9
Number of events		110			

		Cumulative Abnormal Returns			
Day		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	1.44%	1.55	0.79	0.76
2-Day Trailing	t - 1, t	1.59%	3.73***	5.9***	4.79***
2-Day Forward	t, t + 1	1.22%	2.26**	3.85***	2.47**
3-Day Window	t - 1, t + 1	1.62%	2.82***	4.3***	3.14***

*$p<.10$
**$p<.05$
***$p<.01$

Table 12: Event Study Analysis (1996-2005 sample)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0.22%	0.83	0.44	0.32
	t-4	0.09%	0.40	0.52	0.48
	t-3	0.15%	0.63	-0.05	-0.04
	t-2	0.12%	0.62	0.52	0.52
	t-1	0.14%	0.67	0.86	0.82
	Event day	1.25%	3.71***	6.19***	4.14***
	t+1	0.62%	2.11**	4.14***	3.17***
	t+2	-0.38%	-1.88*	-1.20	-1.14
	t+3	0,00%	-0.01	-0.07	-0.08
	t+4	0.1%	0.43	1.12	1.01
	t+5	-0.07%	-0.41	-0.15	-0.17
Number of events		187			

Day		Cumulative Abnormal Returns			
		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	0.78%	0.94	1.47	1.62
2-Day Trailing	t - 1, t	1.41%	3.53***	4.99***	3.92***
2-Day Forward	t, t + 1	1.89%	4.08***	7.37***	5.15***
3-Day Window	t - 1, t + 1	2.03%	3.96***	6.41***	4.79***

*$p<.10$
**$p<.05$
***$p<.01$

Table 13: Event Study Analysis (2006-2015 sample)

		Abnormal Returns			
	Day	Abnormal return	t-stat	Patell's test	Std. z-stat
	t-5	0.06%	0.33	0.03	0.02
	t-4	0.19%	1.46	0.67	0.74
	t-3	0.17%	1.1	1.68	1.61
	t-2	0.17%	0.96	0.8	0.73
	t-1	-0.07%	-0.57	-0.29	-0.32
	Event day	0.74%	2.50**	4.58***	2.63***
	t+1	4.61%	1.43	14.5***	2.27**
	t+2	-0.45%	-2.87***	-2.45**	-2.40**
	t+3	0.01%	0.04	0.04	0.04
	t+4	0.06%	0.36	0.81	0.69
	t+5	0.04%	0.28	-0.11	-0.11
Number of events		196			

Day		Cumulative Abnormal Returns			
		Cumulative abnormal return	t-stat	Patell's test	Std. z-stat
21-Day Window	t - 10, t + 10	5.93%	1.68	5.80***	3.30***
2-Day Trailing	t - 1, t	0.65%	2.16**	2.99***	2.31**
2-Day Forward	t, t + 1	5.35%	1.65*	13.64***	2.89***
3-Day Window	t - 1, t + 1	5.27%	1.63	10.93***	2.85***

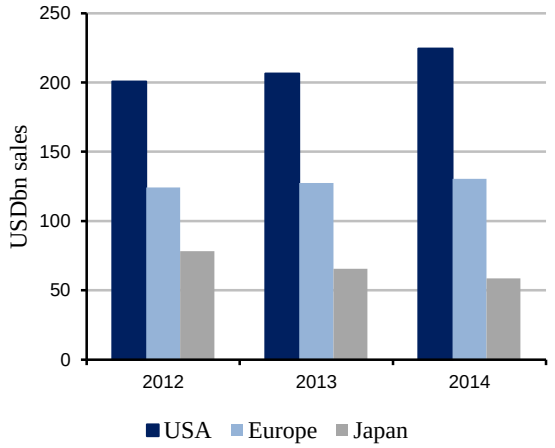
*$p<.10$
**$p<.05$
***$p<.01$

Table 14: Event Study comparisons

Day		Cumulative Abnormal Returns		
		1985-1995	1996-2005	2006-2015
3-Day Window	t - 1, t + 1	1.62%	2.03%	5.27%

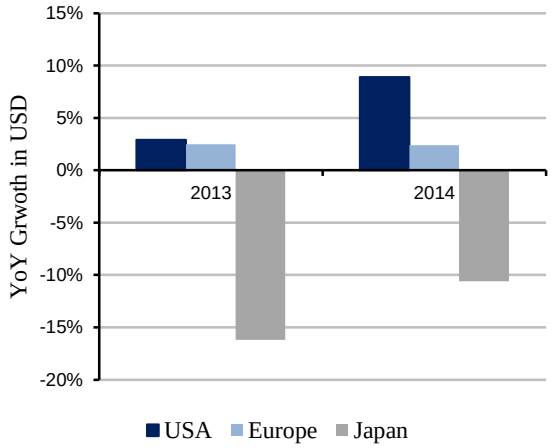
Appendix 9: Figures for the Regression Analysis

Figure 34: 2012 Through 2014 USDbn Sales by Regions



Source: (EvaluatePharma, 2015)

Figure 35: 2013 and 2014 USD branded drug sales growth by Regions



Source: (EvaluatePharma, 2015)

Appendix 10: NAICS Classifications

Table 15: NAICS Classifications

NAICS	Definition
325412	Pharmaceutical Preparation Manufacturing
325414	Biological Product (except Diagnostic) Manufacturing
325413	In-Vitro Diagnostic Substance Manufacturing

Source: (United States Department of Labor, n.d.)

Appendix 11: Regression Results with HK(α)

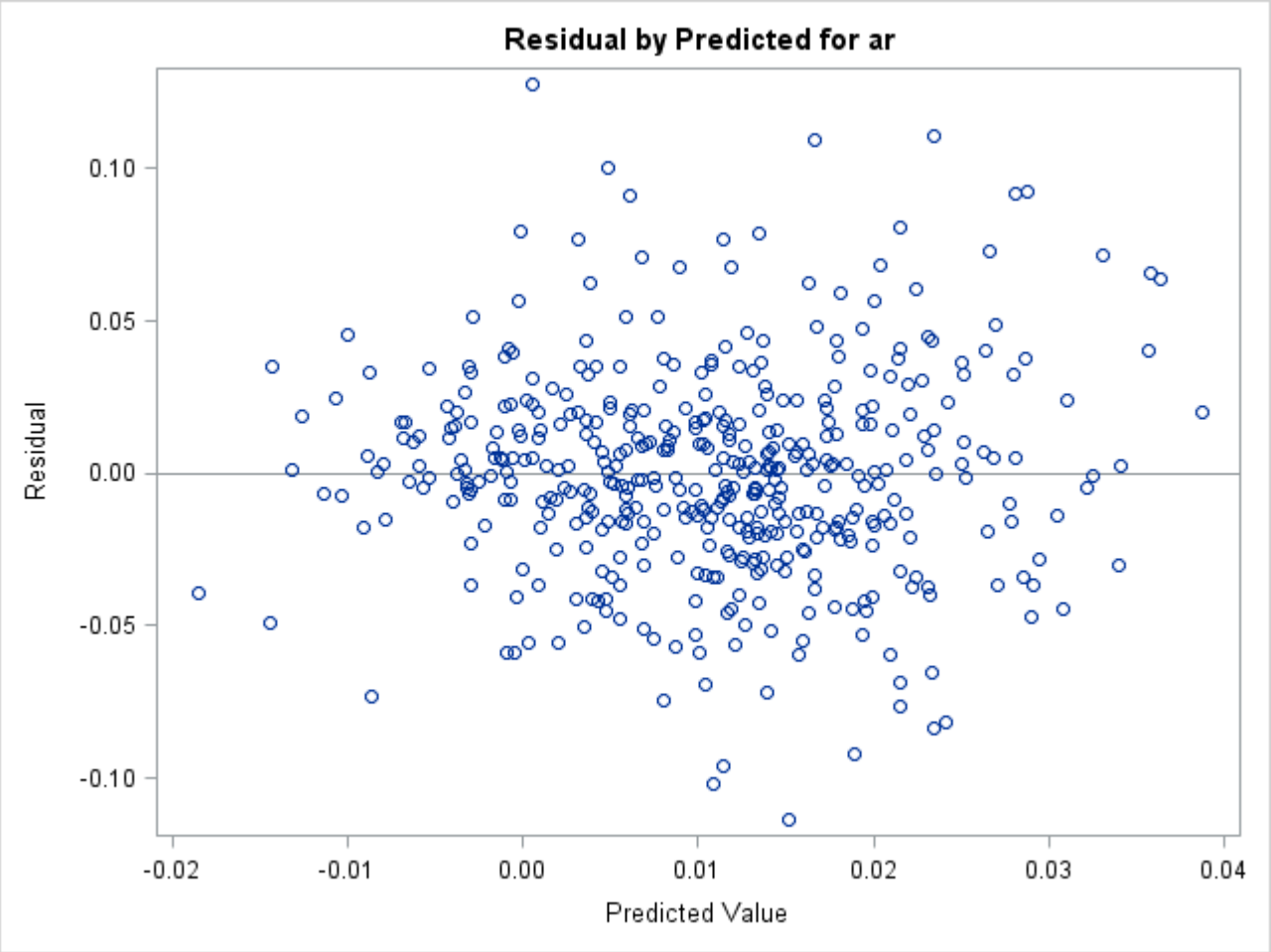
Table 16: Regression Analysis Models of Abnormal Returns

Dependent variable: Abnormal returns; 447 observations	
	Models
Regressors	Model (4)
$Comp_{jt}$	0.336 (0.147)**
$Comp_{jt}^2$	-0.287** (0.134)
$capital\ intensity_{k,t-1}$	-0.002 (0.006)
$growth_{j,t-1}$	0.000 (0.001)
$CDR_{j,t}$	0.018 (0.007)**
$ADS_{j,t}$	0.067 (0.304)
$Cohort_{1996-2005}$	0.170 (0.157)
$Cohort_{2006-2015}$	-0.049 (0.082)
$Comp_{jt} \times Cohort_{1996-2005}$	-0.964 (1.055)
$Comp_{jt} \times Cohort_{2006-2015}$	0.409 (0.543)
$Comp_{jt}^2 \times Cohort_{1996-2005}$	1.214 (1.601)
$Comp_{jt}^2 \times Cohort_{2006-2015}$	-0.899 (0.854)
$R\&D\ intensity_{k,t-1}$	0.087* (0.468)
$labour\ quality_{k,t-1}$	-0.007 (0.005)
$market\ capatilzation_{l,t}$	-0.005 (0.002)
$Joint\ venture_{i,t}$	-0.010** 0.005
$drug\ prioty_{i,t}$	0.007** (0.003)
$Intercept$	-0.048 (0.044)
F-Statistics and *p*-Values on Joint Hypotheses	
(a) Time Variables	0.35 0.555
(b) $Comp$ indicators + all interactions	0.08 0.78
(c) Global *F*-Statistic	1.78** (0.028)
Adjusted $\bar{R}^2$	0.0289

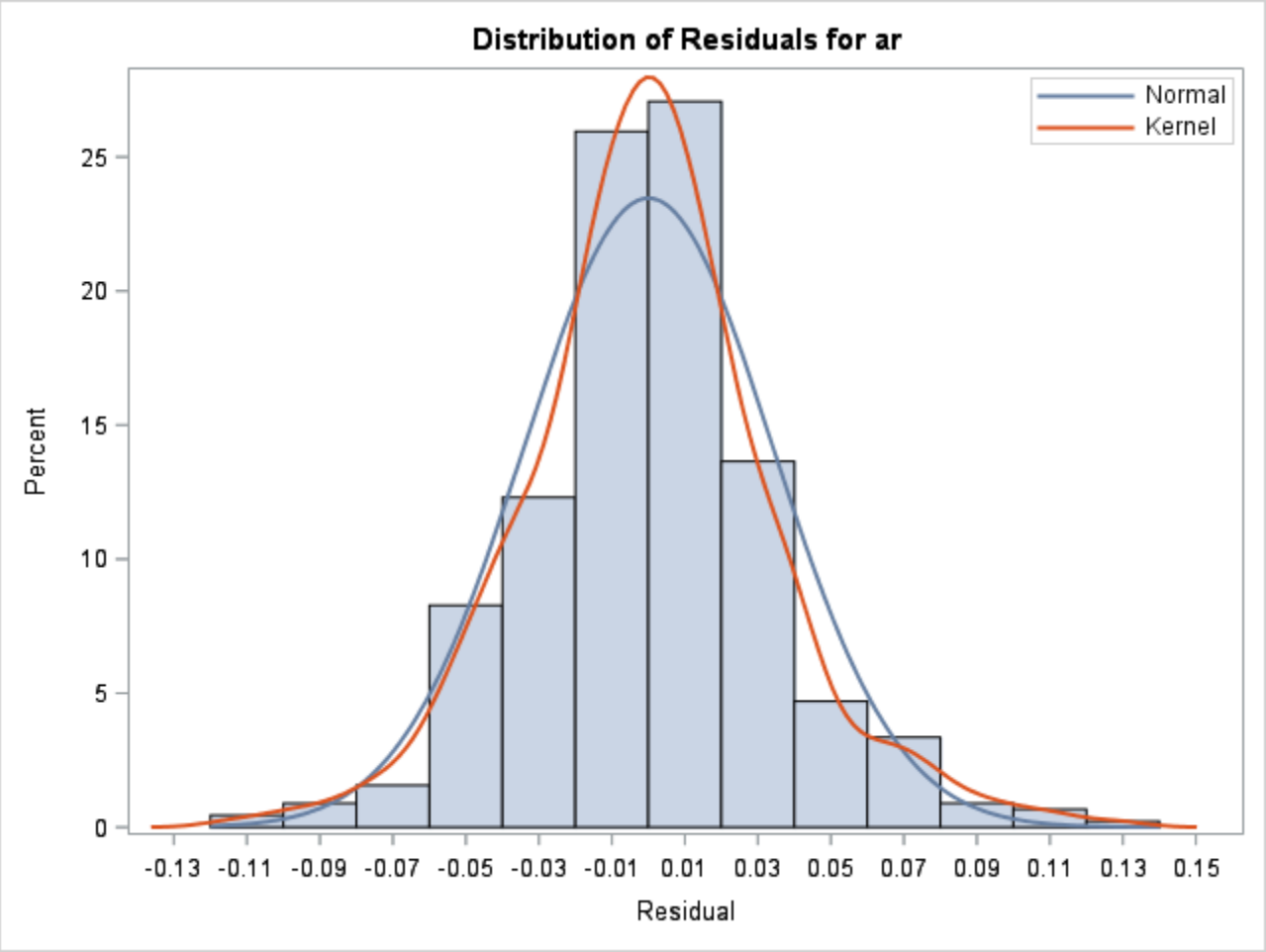
*p<.10; **p<.05; ***p<.01*

Appendix 12: Residual Analysis

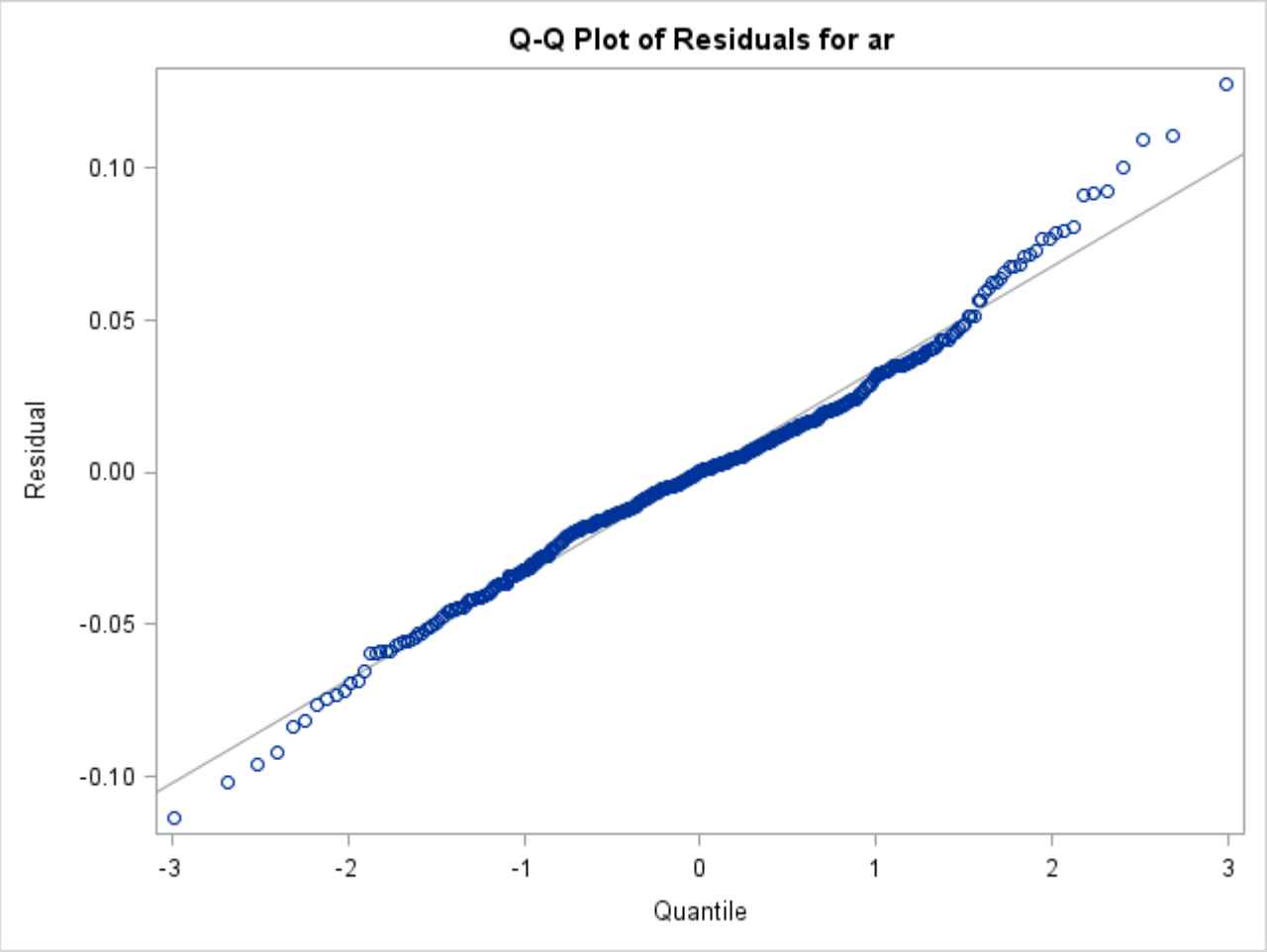
In following appendix a brief residual analysis is carried out.



The above residual plot show that the predicted value tends to cluster around the middle. Furthermore, there is a small sign that the error variance is increasing. Hence, the residual show signs of heteroscedasticity.



The histogram of the Residual shows an approximated symmetric bell-shaped nature. It thus assumed that the normality assumption MLR 6 is true. This indicates that the model's underlying normality assumption also is true.



This is also shown in the Normal Probability Plot of the Residuals.